THE
BRITISH JOURNAL OF SURGERY

VOL. XIX. OCTOBER, 1931. No. 74.

SOME BYGONE OPERATIONS IN SURGERY.

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VI. AMPUTATION: THE OPERATION ON NELSON IN 1797.

THE history of amputation has still to be written. The operation must always have been necessary, but there does not seem to be any detailed account until Celsus describes it in the last chapter of the seventh book *De Medicina*, and then only in a few lines as a treatment for some cases of gangrene. He recommends what is now called the modified circular operation. The skin and muscles are to be divided and retracted, the bone being sawn through at a higher point. There is no mention of any method of arresting hæmorrhage or of bringing the edges of the wound together. Archigenes, who is mentioned by Juvenal, recognized that amputation was required in cases other than gangrene, but neither he nor Paulus Aegineta, who lived some five hundred years later, altered the time-honoured circular division of the limb, though they stopped the bleeding by applying very hot irons. Amputation, even in cases of gangrene, seems to have fallen into complete disuse amongst the Arabian surgeons, and it was not until the thirteenth and fourteenth centuries that it was revived by Henri de Mondeville and Gui de Chauliac, both of whom used the circular method.

It is certain that the circular method remained in exclusive use for very many years. John Woodall, writing in 1639, says :—

"The amputation once resolved upon and all things ready for the work, let the Surgeon with all his assistances and friends not forget before the beginning of the work heartily to call upon God for a blessing upon their endeavours, and let the patient the day before have notice given him that he also may take time to prepare himself with true resolution of soul and body to undergo the work, as being never performed without danger of death, which done, then let the Surgeon prepare himself also with his helpers, namely at the least five persons besides himself, as for example, one to sit behind the patient to hold him, a second for a holder, who by the surgeon must be instructed to stand fast before him and to bestride the limb to be amputated and to amplect the limb; and a third to hold and stay the lower end of the diseased member

to be taken off; a fourth to receive and bring back the sharp instruments; a fifth, to attend the Artist and deliver to him his needles and buttons, restrictive rollers, bolsters, bladder and so soon as possibly may be to stay with the palm of his hand the medicines applied to the end of the abscissed stump that being the duty of the fifth helper and the sixth is the Artist himself that dismembereth. Six and not fewer are the least for the work of taking off a leg or an arm if it be done in the whole or sound part or for taking off a member proceeding by a wound by Gun-shot, done in the lacerated not totally mortified part. But for the taking off a member in the mortified part three persons as assistants may serve, or two for a need, namely one to hold the upper part, the other the lower end. Let the surgeon have ready for instruments a fit amputating Cerra [saw], a Catlin and a good small incision knife, a good pair of strong scissors and three or four cauterising instruments. Let one of the assistants take the upper part of the member, holding it in both hands reasonably fast and steady. I mean the whole part thereof somewhat near unto the unsound part and let the other helper hold the other part. I mean the putrid part to be abscissed in his hand whilst the Surgeon himself first by circumcising divide the putrid flesh from the bone doing it somewhat near the quick part but not too near it, about an inch full from the quick part that with the Cerra he may come without fear to divide the bone or bones asunder where he is sure they are sphacelated not touching any quick part at all with his sharp instruments which he may observe the certainer to do, if with a Needle he enquire cautiously. Let him also divide betwixt the bones the parts there being lest by lacerating or tearing with the teeth of the Cerra he offend, which done let the Artist amputate the bones."

Amputation was still almost limited to cases of gangrene, for the means of arresting hæmorrhage were crude, difficult, and painful.

Forty years after Woodall had thus described the operation in general use, or perhaps sooner, C. Lowdham, a Devonshire surgeon of whom little is known, was practising an entirely new method, a flap operation. This was adopted by his fellow-countryman James Yonge, who published in 1679, "A new way of amputation and a speedier convenient method of curing stumps than that commonly practised, in which (are) divers other useful matters recommended to the military Chirurgeon." The communication took the form of a letter addressed to Mr. Thomas Hobbs dated from Plymouth, August 3, 1676, and it appeared as pages 108–120 of his pamphlet "Currus Triumphalis, è Terebinthô, or an Account of the many admirable Vertues of Oleum Terebinthinæ." Thomas Hobbs, to whom the letter was written, was Lithotomist to St. Bartholomew's Hospital and Serjeant Surgeon (1687–97) to James II and William and Mary.

The manner of the new operation, says Yonge, was as follows, and the first hints came "from a very ingenious brother of ours Mr. C. Lowdham of Exeter. The Ligatures and Gripe being made after the common manner you are with your Catlin, or some long incision-knife, to raise (suppose it the Leg) a flap of the membranous flesh covering the muscles of the Calf, beginning below the place where you intend to make excision and raising it thitherward of length enough to cover the stump. Having so done turn it back under the hand of him that gripes; and, as soon as you have severed the member, bring this flap of cutaneous flesh over the stump and fasten it to the edges thereof

Currus Triumphalis, è Terebinthô.

OR AN

Account of the many admirable Vertues

OF

Oleum Terebinthinæ.

More particularly, of the good effects produced by its application to recent Wounds, especially with respect to the *Hemorrhagies* of the Veins, and Arteries, and the no less pernicious weepings of the Nerves, and Lymphaducts.

Wherein also, the common Methods, and Medicaments, used to restrain *Hemorrhagies*, are examined, and divers of them Censured.

And lastly, A new Way of Amputation, and a speedier convenient Method of curing Stumps, than that commonly practised, is with divers other useful matters recommended to the Military Chirurgeon,

In Two Letters:

The one to his most Honoured, *James Pearse* Esq; Chirurgeon to His Royal Highness the Duke of *York*, and Chirurgeon General to His Majestie's Navy Royal.

The other, to Mr. *Thomas Hobbs*, Chirurgeon in *London*.

By *JAMES YONGE*.

LONDON,
Printed for *J. Martyn*, Printer to the *Royal Society*, at the Bell in St. *Paul*'s Church-yard. 1679.

by four or five strong stitches and, having so done, clap a dossil of lint into the inferior part, that one passage may be open for any blood or matter that may lodge between. Then lay on a common Defensative Ext. Bole, Sang. Dracon, Mastich, Terræ Sigil. cum alb. ovorum & Aceto and thereto gird it close with your cross bandage and other Compresses after the usual manner."

The surgical world must have been ripe for a change from the circular amputation. The flap operation soon came into use in England in spite of the obscure way in which it had been published. A similar operation was practised by Verduyn at Geneva in 1696, by Sabourin at Geneva, and by Garengeot in Paris, each of whom claimed priority.

Some facts about James Yonge are still available, for he was a remarkable person. Born in 1646, he was the son of John Yonge, a surgeon, and was educated at the Plymouth Grammar School until, in 1656, he was apprenticed to Silvester Richmond of Liverpool, who was surgeon to the King's ship, the *Constant Warwick*. He was appointed surgeon's mate to the *Montagu*, a third-rate of 52 guns (formerly the *Lime*), which was built at Portsmouth in 1654 by Mr. Tippetts. Samuel Pepys says of it on May 2, 1661, "We and our wives all to see the 'Montagu' which is a fine ship." It took part in the bombardment of Algiers in 1662 and was afterwards paid off. Yonge then acted as assistant to an apothecary at Wapping for four months, and subsequently helped his father in practice at Plymouth. In February, 1663, he went to Newfoundland in the *Reformation*, and visited the west coast of Africa in 1664. During a second voyage in 1665 his ship was captured by the Dutch, and he was kept prisoner at Amsterdam until September, 1666. He then returned to Plymouth, where he again practised, but in September, 1668, he revisited Newfoundland, returned to England, and settled at Plymouth in 1670. Here he was appointed Surgeon to the Naval Hospital at a salary of five shillings a day, and in 1674 he was Deputy Surgeon General of the Navy. He was Mayor of Plymouth in 1694, and in 1702 he came to London and presented himself for examination at the Royal College of Physicians, although he had long practised on the licence of the Bishop of Exeter. Of this examination he left an interesting account. It was conducted in Lincoln's Inn Fields at the house of the President, Sir Thomas Millington, and was an ordeal of no perfunctory character. "At four o'clock it began and they held me to it till half past five. When they had done they desired me to withdraw and in 4 minutes called me in and told me they were satisfied with my abilities." When the result had been made known to him, "We sat two hours drinking good ale and claret and talking sometime of news and sometime of art." He corresponded with Robert Hooke, the great experimental philosopher who was then Secretary of the Royal Society. Hooke published two of his letters in the *Lectiones Cutlerianæ*; the first describing the fatal symptoms caused by a bullet swallowed into the lungs is dated 1676; the second on May 5th, 1678, contains his own observations and opinions concerning natural fountains and springs. Both are included in *Early Science in Oxford*, vol. viii, published by Mr. R. T. Gunther in 1931. He was elected a Fellow of the Royal Society on Nov. 3, 1702, and in 1707 he embalmed the body of Sir Clowdisley Shovell, the Admiral who was washed up half-drowned on the beach of Porthellick Cove after his ship, the *Association*, had been wrecked on

the Bishop Rock between Land's End and the Scilly Islands. The Admiral was found by a woman who allowed him to die for the sake of a valuable emerald ring which he was wearing. Yonge died on July 25, 1721, and was buried in St. Andrew's Church, Plymouth.

The flap operation thus introduced soon underwent many modifications. The single flap was replaced by double flaps, and the method, at first restricted to the leg, was extended to the other limbs. Liston and Fergusson were its great advocates in England, Liston being so whole-heartedly devoted to it that in his *Elements of Surgery* he entirely omits mention of the circular amputation, though he describes it somewhat grudgingly in his *Practical Surgery*. Speed was of the utmost importance in amputating before the use of anæsthetics, and in the hands of master surgeons like Liston and Fergusson the flap operation was a little quicker than the circular amputation, though in the naval and military services, especially when the operation was required after gunshot wounds and the shattering accidents which were not uncommon on board ship, the circular method remained in favour.

(*To be continued*)

STRANGULATED HERNIA: A REVIEW OF 1487 CASES.

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THE case records upon which the subject-matter of this paper is based were obtained from a large number of surgical centres for the purpose of a collective investigation instigated by the Association of Surgeons of Great Britain and Ireland.

In the case of inguinal and femoral hernia the criterion of strangulation has been the presence of some or all of the symptoms of absolute constipation, pain, and vomiting, and—*more important*—evidence at operation of some interference with the blood-supply of the contents of the sac. Cases of simple obstruction in a hernia without strangulation, cases treated by taxis alone, and cases in which the hernia spontaneously reduced under the anæsthetic have been excluded. In considering umbilical hernia the same criterion has been used as far as possible, though some difficulty has been experienced in excluding cases in which obstruction rather than strangulation was present.

INGUINAL HERNIA.

The total number of cases under review is 654, of which 581 were in males and 73 in females.

Age Incidence and Mortality.—*Table I* shows the age incidence and mortality at various ages: an exceptionally large number of cases is recorded among infants; in other respects the incidence conforms with the usually accepted figures — the greater number occurring in the periods after 40. The mortality rises steadily with increasing age, and among women (17·8 per cent) is considerably higher than among men (12·0 per cent).

Table I.—STRANGULATED INGUINAL HERNIA. AGE INCIDENCE AND MORTALITY.

Males, 581 (70 died). Females, 73 (13 died).

YEARS	CASES	DEATHS
0–2*	38	2
2–5	7	0
6–10	5	0
11–20	27	1
21–30	66	2
31–40	54	2
41–50	100	7
51–60	124	23
61–70	142	23
71–80	75	17
Over 80†	16	6

* Youngest, 7 days (died). † Oldest, 90 years (recovered).

Special Types of Hernia.—The types of hernia met with were as follows: oblique 636, direct 18; of these, 31 were recurrent herniæ (oblique 27, direct 4), and of the recurrences one direct hernia strangulated on its fourth recurrence, having been strangulated twice before. In one case the patient, an infant, had a bilateral

strangulated oblique inguinal hernia, and in one case in addition to the strangulation of an inguinal hernia a similar condition was present in a femoral hernia.

Duration.—In 621 cases in which this information was recorded the *duration of the hernia* before strangulation was as follows: Less than one year, 63 (including 31 infants of less than one year); more than one year, 491; strangulation was the first sign of the presence of a hernia in 67. Primary strangulation, although slightly more common in the third and fourth decades, occurred in patients of all ages except in infants.

The duration of symptoms before operation is shown in *Table II*, together with the death-rate for the various periods of time. It will be seen that, apart from medical complications and accidents, the mortality in the first twenty-four hours is comparatively low, but that after this period a rapid rise in death-rate obtains. Of the 20 deaths occurring in the first three periods (up to eighteen hours), 12 died from conditions consequent on or aggravated by the operation, and not as an immediate result of the strangulation, the cause of death in these cases being: Pneumonia 4, cardiac lesion 2, uræmia 2, hæmatemesis 1, embolism 1, chloroform 2.

Table II.—Strangulated Inguinal Hernia. Duration of Symptoms before Operation, with Deaths.

Duration	Cases	Deaths
Hours		
0–6	125	4
7–12	149	11
13–18	35	5
19–24	104	5
25–36	19	6
Days		
2	61	16
3	29	8
4	30	12
5	11	4
6	3	0
7	5	1
8	1	0
14	2	1
Duration not stated	80	10
Total ..	654	83

Symptoms.—The symptoms noted in detail in 606 case sheets show no remarkable feature: *pain, vomiting, and constipation* were noted in 424 cases; *pain alone or pain and constipation* in 168 cases, of which 34 were instances of strangulated omentum only. *Persistent vomiting* as the sole symptom was noted in 14 cases, including 3 of strangulated intestine in infants, 3 of strangulated omentum in adults, and 4 of strangulation of large intestine or cæcum.

In 20 cases definite *stercoraceous vomiting* was recorded, and of these no fewer than 15 recovered after operation: this appears to cast some doubt on the statement, so frequently made, that stercoraceous vomiting is always a presage of a fatal issue in cases of intestinal obstruction.

A grave degree of *shock* was noted in 6 cases—all in young men in whom the hernia had come down for the first time and presumably due to the sudden stretching of the sensitive parietal peritoneum at the neck of the sac.

Site of Strangulation and Contents of Sac.—The site at various ages is indicated in *Table III*: the comparative frequency of strangulation at the external ring in infants and the gradual increase of frequency of this site with advancing years is noteworthy. Besides those recorded in the table, in 5 cases strangulation resulted from the presence of a band within the sac.

The contents of the sac are given in *Table IV*, which is self-explanatory. One case alone calls for comment, that of a child aged 3 months, where the contents of the sac was strangulated omentum only.

Table III.—Strangulated Inguinal Hernia. Site of Strangulation in 497 Cases.

Age	Neck of Sac	External Ring
0–2	17	17
2–10	3	1
11–20	27	0
21–30	47	6
31–40	25	11
41–50	70	7
51–60	78	15
61–70	74	18
71–80	49	16
Over 80	11	5
Total ..	401	96

Unusual Types. — Unusual types of hernia occurring in the total series of 654 cases were as follows :—

1. *Interstitial hernia*: 6 cases (0·9 per cent). In 3 cases the testis was imperfectly descended and in 2 it was normal. The remaining case occurred in a woman. (The site of strangulation in these cases was in the secondary sac.) All recovered.

2. *Littre's* hernia*: 4 cases (0·6 per cent). In one instance the Meckel's diverticulum was resected, in the others it was replaced without treatment. All recovered.

Table IV.—Strangulated Inguinal Hernia. Contents of Sac.

Small intestine	433
Small intestine and omentum	61
Small intestine and cæcum and appendix ..	1
Small intestine and appendix	3
Small intestine and sigmoid	2
Small intestine and uterus	1
Small intestine and bladder	6
Large intestine	6
Large intestine and omentum	9
Cæcum and appendix	17
Appendix	1
Appendix and omentum	1
Omentum only	41
Meckel's diverticulum	4
Uterus	1
Appendix epiploica	1
Sliding hernia of cæcum	8
Contents of sac not recorded	58

3. *Richter's hernia*: 15 cases (2·2 per cent). Of these, 6 were treated by simple herniotomy and all recovered: 3 required local repair to the strangulated gut in addition—of these, 2 recovered and 1 died; 1 case was treated by enterostomy and subsequent resection with success. In 2 cases a primary resection was successfully performed. In 3 the abdomen was opened for the treatment of intestinal obstruction of undiagnosed cause, with 2 deaths.

* This type of hernia was first described by Alexis L. Littre (b. 1658) in a paper entitled "Observation sur une nouvelle Espèce de Hernie" published in 1700 (*Mém. de l'Acad. roy. des Sci.*, Paris, 1700). There is no justification for the addition of an accent on the terminal *e* of this distinguished surgeon's name, although this error has been continued in countless text-books and articles during the last hundred years.

4. *Maydl's hernia*: 4 cases (0·6 per cent), with 3 recoveries. Resection of the re-entering loop was required in one patient, who survived.

5. *Reduction en masse*: 4 cases (0·6 per cent) were reported, with 3 deaths. In all cases a resection had to be performed.

Operations.—In *Table V* details are given of the operations performed in 651 out of the 654 cases under review: 3 patients died before any operation could be undertaken.

Table V.—Strangulated Inguinal Hernia. Details of Operations Performed.

	Cases	Deaths
Herniotomy without special operative treatment to bowel	578	46
Herniotomy with precautionary lateral anastomosis ..	2	0
Herniotomy with doubtful gut left unreduced	2	1
Primary drainage of gangrenous loop	10	7
Local repair of damaged bowel wall	15	4
Local repair of damaged bowel wall with lateral anastomosis	1	0
Primary resection of gangrenous bowel	30	14
Primary resection of gangrenous bowel with temporary enterostomy..	3	2
Laparotomy for reduction *en masse*	4	3
Laparotomy for undiagnosed Richter's hernia	3	2
Laparotomy for double hernia, the side strangulated being in doubt	2	1
Local drainage of abscess in sac	1	0
Died before operation could be undertaken	3	3
Total	654	83

Secondary enterostomy was also performed subsequent to the initial operation in 4 cases, with 3 deaths.

Among the 578 cases of *simple herniotomy* where no special treatment of the affected bowel was necessary the following points are of interest:—

1. *The Omentum.*—Congested, strangulated, or adherent omentum was removed in 69 cases with no ill effect or subsequent complication. The risks of spreading thrombosis, hæmorrhage, or necrosis after this proceeding appear to be minimal.

2. *The Testicle.*—In 24 cases a testicle was removed—in 15 instances because it was imperfectly descended, and in 9 owing to damage to the blood-supply. One imperfectly descended testicle was grafted into the patient after removal.

3. *The Bladder.*—Accidental injury to the bladder occurred on 3 occasions: in each the injury was detected at the time and suitably treated with success. No case of undiagnosed injury to the bladder is recorded.

4. *Operation on the Wrong Side.*—In one case, of a man with a large tense hydrocele filled with altered blood on one side and a small strangulated hernia on the other, the hydrocele was explored under the impression that it was a strangulated hernia and was the cause of the symptoms. The patient's condition did not allow of any further operation and he died.

5. *Reduction en Masse at the Time of Operation.*—This accident occurred in one case—it was not detected—with a fatal result.

6. *Fæcal Fistula.*—In one case a fæcal fistula developed at the site of the herniotomy wound; this closed spontaneously.

7. *Internal Strangulation.*—In 2 cases internal strangulation by a band occurred on the sixth and tenth days respectively after the original operation. This condition was successfully relieved by laparotomy in one case.

In considering the 73 cases in which *something more than a simple herniotomy* was required it will be seen that enterostomy, whether primary, secondary, or precautionary (as after excision), is associated with a very high mortality, as must be the case in dealing with desperate conditions. It would, however, appear possible that more cases could be saved if a temporary enterostomy, a foot or more above the site of strangulation, were performed more frequently as a primary measure in cases showing considerable distension of the intestine, and also if a similar method were adopted as an additional measure in cases unfit for resection and treated hitherto by simple drainage of the gangrenous loop.

Of the *enterostomy operations*, one, a secondary enterostomy, is of particular interest. The patient, an infant of 2 months, came under treatment for bilateral strangulated hernia; a double herniotomy was performed with success, but unfortunately on the fourth day the hernia recurred on the right side and again strangulated. The child's condition being desperate, an enterostomy was performed by means of cautery puncture of the scrotal contents, the manœuvre being based on the practice in vogue among certain native tribes. The child recovered.

Little comment is required concerning the other operations performed: the cases of resection will be considered later in the paper together with those necessitated in the treatment of other forms of hernia.

It is of interest to note that where a simple herniotomy alone was necessary the mortality was 7·9 per cent, whereas as soon as any further method of treatment was required owing to injury to the bowel wall, etc., the mortality rose to slightly over 50 per cent.

The Cause of Death.—The cause of death in the 83 fatal cases can be fairly divided into two groups: (1) Causes directly consequent on the condition for which the operation was performed; (2) Causes due to complications which may follow any operation or due to intercurrent maladies.

In Group 1 the following causes of death were noted:—

Ileus	6
Toxæmia	17
Peritonitis	13
Shock	18
Cause not definitely stated ..	5
	59

In Group 2 deaths were assigned as follows:—

Pneumonia	12
Bronchitis	3
Cardiac lesions	1
Uræmia	2
Hæmatemesis	1
Pulmonary embolism	3
Anæsthetic	2
	24

The gross mortality for the 654 cases under review was 12·6 per cent.

FEMORAL HERNIA.

Case records were received of 680 patients, of whom 144 were males and 536 females.

Age Incidence and Mortality.—*Table VI* shows the age incidence and mortality at various ages: the rise in mortality with age is practically the same as in inguinal hernia, but the mortality among men is in the case of femoral hernia far higher than in women (males 22·9 per cent, females 10·2 per cent), whereas the reverse applied in inguinal hernia.

Table VI.—Strangulated Femoral Hernia. Age Incidence and Mortality by Age.
Males, 144 (33 died). Females, 536 (55 died).

Years	Cases	Deaths
11–20*	6	0
21–30	29	2
31–40	77	3
41–50	126	9
51–60	155	15
61–70	194	37
71–80	77	16
Over 80†	16	6
Total ..	680	88

* Youngest, 12 (recovered). † Oldest, 86 (recovered).

Duration.—In 18 cases the hernia when strangulated had recurred after a former operation, and in 2 instances an operation for strangulation had been performed previously. *The duration of the hernia* prior to strangulation was recorded in 550 cases; in 84 patients it had been present for less than one year: in 358 for more than one year, and in 108 strangulation was the first sign of the presence of a hernia.

Table VII.—Strangulated Femoral Hernia. Duration of Symptoms, with Deaths.

Duration	Cases	Deaths
Hours		
0–6	58	3
7–12	72	3
13–18	25	3
19–24	114	1
25–36	24	12
Days		
2	92	9
3	79	18
4	49	8
5	30	8
6	10	2
7	24	5
9	3	2
10	1	1
14	4	1
21	2	0
30	1	0
42	1	0
Duration not stated	91	12
Total ..	680	88

In *Table VII* is shown the *duration of symptoms* before operation and the death-rate for the various periods of time. Here also, as in inguinal hernia, the mortality is low for the first twenty-four hours and then rises rapidly. It will be observed that in a very much larger number of cases than in inguinal hernia the symptoms had been present for forty-eight hours or more; this is difficult to explain, as it would be expected that the rigid femoral canal would produce symptoms of strangulation of sufficient urgency to call for earlier intervention. In a certain proportion (30 per cent) of these cases of long-standing strangulation the contents of the sac was omentum or gut and omentum, in which latter case

the omentum serves to some extent to protect the gut from injury. Similarly the hernia was of the Richter type in 44 cases in which the damage was localized to a small area of the bowel wall, and the symptoms were consequently less severe at first. A large number of cases, however, still remain in which it is difficult to explain the delay in the patient's seeking surgical aid unless the tightness of the strangulation is actually less acute than appears to be the case from an anatomical point of view. An argument against the latter suggestion is the fact that in femoral hernia a considerably higher percentage of cases required special operative treatment for damage to the bowel wall than in inguinal hernia and the resection-rate was considerably higher.

Symptoms.—The symptoms recorded in 615 cases are almost exactly comparable with those occurring in strangulated inguinal hernia. *Pain, vomiting, and constipation* was noted in 493 cases; *pain and constipation* in 117 cases, of which 48 were cases of strangulated omentum. *Persistent vomiting* without other marked symptoms was the feature in 3 cases, and in one instance the vomiting persisted for six weeks before operation for a strangulated hernia of the sigmoid and small intestine, which were both described as being 'extremely congested'.

Visible peristalsis was noted in one case of strangulation of small intestine; the gut at operation was found to be gangrenous. In one case the most pronounced symptom was the presence of an *abscess* in the sac, which after incision developed into a fæcal fistula; in one case the patient came under observation with a *fæcal fistula* at the site of the hernia.

Stercoraceous vomiting was noted in 26 cases, with 9 deaths and 17 recoveries: the high rate of recovery, as in the inguinal cases, is remarkable.

Site of Strangulation and Contents of Sac.—A note was made of the site of strangulation in 525 case sheets, namely:—

Neck of sac and structures surrounding it ..	320
Neck of sac and Gimbernat's ligament ..	29
Gimbernat's ligament	174
Saphenous opening	1
Adhesions in sac	1

It will be seen from these figures that in the larger number of cases strangulation is produced by the neck of the sac and the structures in its immediate neighbourhood, of which the 'deep crural arch' is probably the most important. In old-standing cases, where the neck of the sac has been stretched to some extent by the long-continued presence of a hernia, two other anatomical structures become of importance, i.e., Hey's ligament or the upper edge of the saphenous opening, over which the hernia turns as it passes upwards and outwards after traversing the crural canal, and Gimbernat's ligament, the sharp edge of which acts almost as a knife-edge in its pressure against the protruded gut. These two ligaments act together, the hernia being first fixed by Hey's ligament, and then as it increases in size being pressed against the edge of Gimbernat's ligament. It is open to question whether Gimbernat's ligament is ever the sole cause of strangulation, or whether it is necessary to divide this ligament in any case in which the inguinal method of approach is used: free division of the neck of the sac

from above and below and of Hey's ligament should be sufficient to allow of reduction. Division of Gimbernat's ligament adds greatly to the difficulty of satisfactory repair of the canal.

The contents of the sac are given in *Table VIII*. The only point requiring comment is the large proportion of cases in which omentum was present either with or without intestine as compared with inguinal hernia—namely, 273 cases out of 639 in the case of femoral and 112 cases out of 616 in the case of inguinal hernia. Where omentum and intestine were both contained in the sac it is remarkable that in a considerable proportion of the cases the omentum was more severely affected than the gut, which had presumably been protected by the presence of the omentum.

Table VIII.—Strangulated Femoral Hernia. Contents of Sac.

Small intestine	339
Small intestine and omentum ..	164
Small intestine and appendix ..	4
Small intestine and sigmoid ..	2
Small intestine and bladder ..	3
Large intestine	4
Large intestine and omentum ..	1
Cæcum	2
Cæcum and appendix	4
Appendix alone	4
Omentum alone	106
Omentum and bladder	2
Meckel's diverticulum	1
Appendix epiploica	3
Contents not stated	41
Total	680

Special Types of Hernia.—

Littre's hernia: In the one case in which a Meckel's diverticulum was strangulated a successful result followed excision of the diverticulum.

Richter's hernia: 77 cases of this type of hernia were noted, forming an unexpectedly high percentage (11·3 per cent) of the total number. Of these, 62 recovered and 15 died. In 75 cases the small intestine was involved, in 1 the caput cæci, and in 1 the sigmoid. Thirty-nine cases were treated by simple herniotomy, with 5 deaths: in 19 cases, in addition to the herniotomy, local repair was required to the wall of the intestine; of these, 18 recovered and 1 died. Resection of the damaged intestine was necessary in 11 cases, with 4 deaths. Six cases were treated by exploratory laparotomy for an undiagnosed acute intestinal obstruction: of these, 4 died. One case was operated on under the impression that the condition was an acute abscess, perforation having occurred into the sac; this patient eventually recovered. One case was moribund on coming under observation and died without operation. It is noteworthy that approximately 60 per cent of the cases of Richter's hernia did not come under treatment until the condition had been present for forty-eight hours or more.

Operations.—The various operations performed in 679 cases are shown in *Table IX*. One patient was moribund on admission to hospital and no operation could be undertaken. The records do not always indicate clearly the type of operation that was performed or the mode of access, but in

616 cases in which a definite statement is made the following methods were employed :—

Femoral route (Lockwood's operation, etc.) ..	285
Inguinal route (Lotheisen type of operation) ..	319
Hey Groves's operation	12

As is shown by the figures, the operation by the femoral route still has its advocates who claim that for a life-saving operation this method is the better as it is simple and quick. The comparative simplicity and rapidity of the operation are, however, outweighed by the greater certainty of cure given by the inguinal operation, and more especially by the fact that with this latter operation the strangulated intestine can be examined more adequately and a resection can be performed without making any further incision.

It may be noted that on 24 occasions, in addition to an operation by the femoral route, a laparotomy had also to be performed in order to inspect doubtful gut which had slipped back during the operation, or to remove an inflamed appendix or to carry out a resection : these additional operations would not have been necessary if the inguinal route had been utilized.

Table IX.—Strangulated Femoral Hernia. Details of Operations Performed.

	Cases	Deaths
Herniotomy without special operative treatment to bowel	551	42
Herniotomy with precautionary lateral anastomosis ..	3	1
Herniotomy with doubtful gut left unreduced	2	2
Herniotomy with temporary enterostomy	3	1
Primary drainage of gangrenous loop	11	10
Local repair of damaged bowel wall	35	4
Local repair of damaged bowel wall with lateral anastomosis	4	1
Local repair of damaged bowel wall with temporary enterostomy	1	0
Primary resection of gangrenous bowel	57	21
Primary resection of gangrenous bowel with temporary enterostomy	2	1
Secondary resection after primary lateral anastomosis, gangrenous bowel being left outside abdomen ..	1	0
Laparotomy for undiagnosed acute obstruction ..	7	4
Drainage of abscess in sac with subsequent fæcal fistula ..	2	0
No operation : patient moribund	1	1
Total	680	88

Laparotomy was also performed in 4 cases to inspect intestine which had slipped back during herniotomy, for the removal of an inflamed appendix, etc.

1. *The Omentum.*—Affected omentum was removed at operation on 120 occasions with no apparent ill effect or complication afterwards : as a similar satisfactory result was obtained in the inguinal cases it would appear that the reputed dangers of hæmorrhage, spreading thrombosis, or interference with the transverse colon are negligible.

2. *Empty Sac.*—In 3 cases presenting all the typical symptoms and signs of strangulation, at operation the sac was found to contain nothing further than fluid under tension. This condition, which is not very uncommon, is difficult to explain, but it seems possible that temporary blockage of the

uppermost part of the neck of the sac may have resulted from the apposition to it of a tag of omentum or of a portion of bowel—in the latter case the condition would really be the early stage of a Richter's hernia. On opening the sac from below it is obvious that no contents other than fluid would be found and it would be difficult to detect the original cause of the trouble.*

3. *The Bladder.*—An injury to the bladder necessitating a local repair was noted in 4 cases, all of which recovered.

4. *Abnormal Obturator Artery.*—The abnormality of an obturator artery running along the free edge of Gimbernat's ligament was noted in 3 cases and dealt with by ligature at the time of operation.

5. *Acute Intestinal Obstruction.*—In one case of simple herniotomy acute intestinal obstruction from an omental adhesion to the site of strangulation on the intestinal wall occurred on the fourteenth day. This was treated by laparotomy with success: a further obstruction occurred on the twentieth day from the same cause, and was again successfully treated by laparotomy with recovery of the patient. In this case at the original operation the sac contained gut only.

The number of cases requiring something *more than a simple herniotomy* was considerably larger in femoral hernia as compared with inguinal (76 in inguinal, 128 in femoral). This difference was almost entirely due to the increased number of cases requiring local repair to damaged bowel wall and to the greater number of resections, and this increase can be attributed to the large numbers of the Richter type of hernia in which severe damage may occur to a portion of the bowel and also to the serious injury produced by the pressure of the sharp edge of Gimbernat's ligament in the ordinary type of hernia. The actual technique of the repair of damage to the intestinal wall varied with the individual case, but mention may be made of the danger of invaginating a constriction ring involving the whole circumference of the bowel. In 5 cases in which this method was adopted intestinal obstruction occurred within a few days, necessitating a further operation in each case and with a fatal result in 2 cases out of 5. It would appear to be a safer proceeding to perform a resection as a primary operation or to exclude the damaged area, after such a repair, by a lateral anastomosis.

The very high mortality obtaining in cases treated by simple drainage of the gangrenous loop suggests that in this condition local drainage is not sufficient, and that some diminution in the mortality might occur if the bowel were drained above the site of the obstruction as well as locally.

The two cases of abscess in the sac are of interest. In one, what appeared to be an acute abscess in the groin was opened, pus was evacuated, and a fæcal fistula developed shortly afterwards: this fistula closed without further treatment. In the second case the abscess burst spontaneously before the patient came under observation, and a fæcal fistula developed: this condition was treated by laparotomy and exclusion of the affected portion

* In a case of this type recently operated on by the inguinal route, on deliberately opening the peritoneal cavity a loop of intestine with a small circular congested area on its antimesenteric border was noted. This bears out the theory that this condition is an early stage of a Richter's hernia.

of gut (cæcum) by lateral anastomosis followed by a resection of the cæcum and a portion of the ascending colon and ileum at a later date with success.

A consideration of the cases of resection is deferred till later in the paper.

The mortality for the cases of simple herniotomy was 7·6 per cent, whereas in cases requiring more than simple release of the strangulated gut the mortality rose to 35·1 per cent.

The Cause of Death.—Using the same classification as in inguinal hernia the causes of death were as follows :—

1. Causes directly consequent on the condition for which the operation was performed :—

Ileus	10
Toxæmia	30
Peritonitis	15
Shock	8
Causes not definitely stated ..	6
Total	69

2. Causes due to complications which may follow any operation or due to intercurrent maladies :—

Pneumonia	13
Uræmia	1
Pulmonary embolism	4
Anæsthetic	1
	19

The gross mortality for the 680 cases under review was 12·9 per cent.

UMBILICAL HERNIA.

Case sheets were received dealing with 153 patients, of whom 23 were males and 130 females.

Age Incidence and Mortality.—*Table X* gives the age incidence and mortality for various ages : the single instance of strangulation of an umbilical hernia in an infant is included, as in spite of the extreme youth of this patient the case appears to have been one of a true strangulated hernia. The maximum rate of incidence is between 50 and 70 years.

Table X.—Strangulated Umbilical Hernia. Age Incidence and Mortality by Age.

Males, 23 (12 died). Females, 130 (50 died).

Duration	Cases	Deaths
1 day	1	0
31–40 years	5	2
41–50 ,,	19	1
51–60 ,,	58	23
61–70 ,,	50	28
71–80 ,,	18	7
Over 80 ,,	2	1
Total ..	153	62

Strangulation occurred in *recurrences* after a previous operation in 21 cases, and in 2 instances the hernia had already been operated upon for strangulation.

In only 14 cases had the hernia been present for less than one year ; and in 6 of these patients the hernia strangulated at its first appearance.

Duration.—The duration of symptoms before operation is given in *Table XI*, together with the deaths for each period. Of the cases with long-standing symptoms in which recovery took place, the contents of the sac consisted of omentum only or of large gut and omentum: no case of strangulation of small intestine of a duration exceeding 2 days recovered.

Table XI.—Strangulated Umbilical Hernia. Duration of Symptoms.

Duration	Cases	Deaths
Hours		
0–6	7	3
7–12	16	1
13–18	8	4
19–24	28	6
25–36	8	3
Days		
2	16	12
3	17	3
4	12	8
5	6	6
6	2	2
7	4	2
14	1	0
Duration not stated	28	12
Total ..	153	62

Symptoms.—The symptoms recorded presented no noteworthy feature except that of the 14 patients noted as having *stercoraceous vomiting* before operation no fewer than 8 recovered. This recovery-rate conforms with that found in strangulated inguinal and femoral hernia and helps still further to refute the usually accepted hopeless prognosis of such a condition.

Cause of Strangulation and Contents of Sac.—The cause of strangulation in 136 cases in which this fact was recorded was as follows:—

Neck of sac	109
Band within sac ..	6
Saccule within sac ..	18
Implanted filigree ..	3

Strangulation in a saccule within the sac is of importance as the clinical signs of strangulation in the hernia itself may be absent or negligible, especially if the hernia is large and the saccule is small and deeply placed. The existence of this condition, which is not uncommon in umbilical hernia, should therefore always be borne in mind.

The contents of the sac are given in *Table XII*. The most remarkable feature presented in this is the fact that small intestine or small intestine

Table XII.—Strangulated Umbilical Hernia. Contents of Sac.

Small intestine	48
Small intestine and omentum	43
Large intestine and omentum	16
Large and small intestine and omentum ..	27*
Omentum	12
Contents not stated	7

* In 24 cases the small intestine alone was strangulated.

and omentum formed the contents of the sac rather more than six times as often as large intestine and omentum. It would also appear that where small intestine was found in a sac together with large intestine and omentum

the former had clearly been the last structure to enter the sac, the omentum and colon being as a rule fixed by old adhesions. Further, when small intestine and colon were both contained in a sac the former was almost always alone affected by the strangulation: in 3 only out of 27 cases of this type of hernia was the large intestine involved to any extent.

Of the 12 cases in which omentum alone was strangulated, only 1 died as an immediate result of the operation, death resulting from shock.

Several enormous hernias are recorded: in two the contents consisted of several feet of ileum, the cæcum, and the whole of the colon as far as the sigmoid—both died.

Special Types of Hernia.—Two cases of *Richter's hernia* of small intestine are recorded: in one the small intestine alone was involved; in the other omentum was also present—this latter patient died.

Operations.—Details of 150 operations are given in *Table XIII*: 3 patients were moribund on admission and died before any operation could be attempted. Various methods of repair were used, but that of Mayo was employed in the majority of the cases; a filigree was used in one case which recurred within two years. Omentum was removed in 46 cases, again without ill effect, as was the case also in inguinal and femoral hernia.

Table XIII.—Strangulated Umbilical Hernia. Operations.

	Cases	Deaths
Simple herniotomy and repair	114	33
Primary drainage of intestine—small	9	9
Primary drainage of intestine—large	5	5
Primary drainage of intestine—large and small	1	1
Local repair of bowel wall (colon 3, all died)	6	3
Local repair of bowel wall with anastomosis	2	2
Primary resection of gangrenous bowel—small	11	5
Primary resection of gangrenous bowel—large	1	1
Primary resection of gangrenous bowel—cæcum and ileum	1	1
No operation	3	3
Total	153	63

Of the cases requiring *more than simple herniotomy* it will be observed that small intestine was affected in far greater proportion than large, and that in every case requiring repair, drainage, or excision of large intestine the patient died. It is also noteworthy that every case of primary drainage of gangrenous intestine died.

The cases treated by excision are considered later. The mortality for simple herniotomy was 28·8 per cent, whereas in cases requiring treatment other than simple release of the strangulation the mortality rose to 76·1 per cent.

The Cause of Death.—Adopting the same classification as in the other types of hernia, the fatal cases are grouped as follows:—

1. Causes directly consequent on the condition for which the operation was performed.

Shock	28
Toxæmia	17
Peritonitis	4
Cause not stated ..	1
	50

2. Causes due to complications following the operation or to intercurrent maladies.

Pneumonia	..	..	5
Bronchitis	..	..	2
Diabetes	..	..	2
Uræmia	..	..	1
Pulmonary embolism		..	1
Anæsthetic	..	..	2
			13

The gross mortality for all the cases under review was 41·1 per cent.

RESECTIONS.

In the consideration of resections of gangrenous intestine only those cases that were performed at the initial operation are included: secondary resections after preliminary drainage, of which 7 were performed with one death, present an entirely different problem, as no obstruction was present at the time of operation.

Of the 1480 operations performed for strangulated hernia, primary resection was required in 105 cases (7 per cent): 33 cases in inguinal, 59 in femoral, and 13 in umbilical hernia. The high rate in femoral hernia corresponds with the long duration of symptoms before operation already noted as occurring in this condition. This point is also indicated in *Table XIV*, which gives

Table XIV.—Resections. Duration of Symptoms before Operation.

Duration	Inguinal			Femoral			Umbilical		
Hours	Cases	Recovered	Died	Cases	Recovered	Died	Cases	Recovered	Died
0–6	0	0	0	1	1	0	1	0	1
7–12	1	1	0	1	0	1	0	0	0
13–18	3	2	1	3	1	2	0	0	0
19–24	8	6	2	6	5	1	1	0	1
25–36	2	1	1	3	0	3	1	0	1
Days									
2	7	3	4	10	7	3	1	0	1
3	5	0	5	9	6	3	4	4	0
4	4	1	3	7	5	2	1	0	1
5	0	0	0	4	4	0	0	0	0
6	0	0	0	1	1	0	0	0	0
7	1	1	0	0	0	0	0	0	0
Duration not stated	2	2	0	14	7	7	4	2	2
Total ..	33	17	16	59	37	22	13	6	7

the duration of symptoms in each type of hernia before resection was performed. It will be seen in this table that in the majority of cases requiring resection the symptoms had been present for twenty-four hours or more, and that under twenty-four hours this operation was but rarely required.

Apart from 1 case of resection of gangrenous transverse colon and 2 cases of resection of ileum and cæcum, all of which died, the resections were all of small intestine.

The types of anastomosis used were as follows :—

	Number	Recovered	Died	Mortality
End-to-end	44	25	19	43·1 per cent
Lateral	59	35	24	40·6 ,, ,,
End-to-side (ileum to colon)	2	0	2	100 ,, ,,
All types	105	60	45	42·8 ,, ,,

There seems little difference between the two methods of end-to-end and lateral anastomosis, though the latter shows a higher incidence and a slightly lower mortality. In one case of end-to-end anastomosis mechanical obstruction occurred on the fourth day ; this was rectified by a lateral anastomosis.

Temporary enterostomy above the anastomosis was performed on 6 occasions, with 2 deaths : it would appear that a further use of this method might diminish the mortality in cases of resection.

The method of access for the resection varied with the type of case : in 30 out of 33 inguinal cases the resection was performed through the herniotomy wound, whereas in the femoral cases in 21 cases out of 59 a separate laparotomy was performed.

POST-OPERATIVE COMPLICATIONS.
PULMONARY COMPLICATIONS. ANÆSTHETICS.

Post-operative complications apart from thrombosis and affections of the lungs were few in number and trivial in degree, only two cases of parotitis and two of transient delirium being noted.

Pulmonary embolism occurred in 10 cases, with 8 deaths, the earliest case being on the fifth day and the latest on the thirtieth day after operation. No record of the origin of the embolus was given in 8 cases : in 2 the femoral vein was thrombosed—in one case on the same side, and in the other, on the side opposite to that operated on.

Uncomplicated *femoral thrombosis* was noted in 3 cases. Considering the close proximity of the femoral vein to the operation area in both inguinal and femoral hernia, and also that in the majority of cases of strangulation an element of infection is inevitable, the comparatively high rate of incidence of embolism (0·67 per cent) is explicable.

Post-operative pulmonary complications of varying degree were noted in 105 cases out of 1480 operations (7 per cent), with 35 deaths—that is, a death-rate of 33·3 per cent for pulmonary complications *per se*, and of 2·3 per cent from pulmonary complications for all cases of strangulated hernia operated on. The exact lesions produced were difficult to determine, but the following list gives them as accurately as possible :—

	Cases	Deaths
Bronchitis	57	6
Bronchopneumonia ..	36	23
Lobar pneumonia ..	10	6
Massive collapse ..	2	0
Total ..	105	35

It was impossible to exclude from the list cases in which bronchitis, etc., were present before the operation, but it can safely be assumed that any antecedent condition was aggravated by the operation.

Five deaths occurred *during the administration of the anæsthetic*: of these 2 can be fairly attributed to the anæsthetic, as death occurred during induction with chloroform; 2 occurred in desperate cases, and can more properly be attributed to the shock of the operation, and in 1 it is recorded that the patient was drowned in his own vomit during the operation.

The various types of anæsthetic employed, with the pulmonary complications occurring in each type, are given in *Table XV*. In this it will be seen that the anæsthetic of choice was ether: under this heading are included all

Table XV.—Anæsthetics and Pulmonary Complications.

Anæsthesia	Cases	Pulmonary Complications	Incidence	Deaths from Pulmonary Disease
			Per cent	
General, type not stated	116	7	6·0	0
Ether	685	52	7·6	20
C.E. mixture	332	16	4·8	2
Chloroform	33	5	15·0	4
Gas and oxygen ..	68	8	11·0	1
Local	137	12	8·7	5
Spinal	108	5	4·5	3
Avertin	1	0	0·0	0
Total ..	1480	105	—	35

cases which were given mainly ether, a case in which C.E. mixture was given for the induction followed by ether being classed as an ether anæsthetic. The incidence of pulmonary complications after ether corresponds almost exactly with the general incidence, and no serious contra-indication to the use of this safe anæsthetic, if inhalation anæsthesia is employed, can be brought forward. The high incidence after chloroform, gas and oxygen, and local anæsthesia can be attributed to the fact that these methods were in all probability used because of a known pulmonary affection in the patient.

It is an accepted fact that pulmonary complications in acute intestinal obstruction are due in the main to the inspiration of highly infected material vomited from the stomach. Some improvement in the very high rate of incidence of and mortality from such complications should therefore be obtainable by careful lavage of the stomach before and after operation, and by the use of local or spinal anæsthesia in preference to any inhalation method.

SUMMARY.

1. A review of 1487 strangulated inguinal, femoral, and umbilical hernias.

2. The mortality in each group was as follows: Inguinal 12·6 per cent, femoral 12·9 per cent, umbilical 41·1 per cent, and for all cases 15·7 per cent.

3. It was necessary to resect intestine in 105 cases, with 45 deaths.

4. Pulmonary embolism occurred in 10 cases (with 8 deaths) out of a total number of 1480 operations.

5. Pulmonary complications, bronchitis, pneumonia, etc., followed the operation in 105 cases, with 35 deaths.

6. Stercoraceous vomiting was recorded as a symptom in 60 cases, with 40 recoveries and 20 deaths.

A CASE OF GENERALIZED FIBROCYSTIC DISEASE OF THE BONES.

By Lieut.-Colonel E. W. C. BRADFIELD, I.M.S.,
PROFESSOR OF SURGERY, MADRAS.

The patient first came under observation in 1913, when at the age of 6 years he was admitted to the General Hospital, Madras, for a fracture of the right femur. A brief note of his condition was recorded by Mr. Elmslie[1] in 1914.

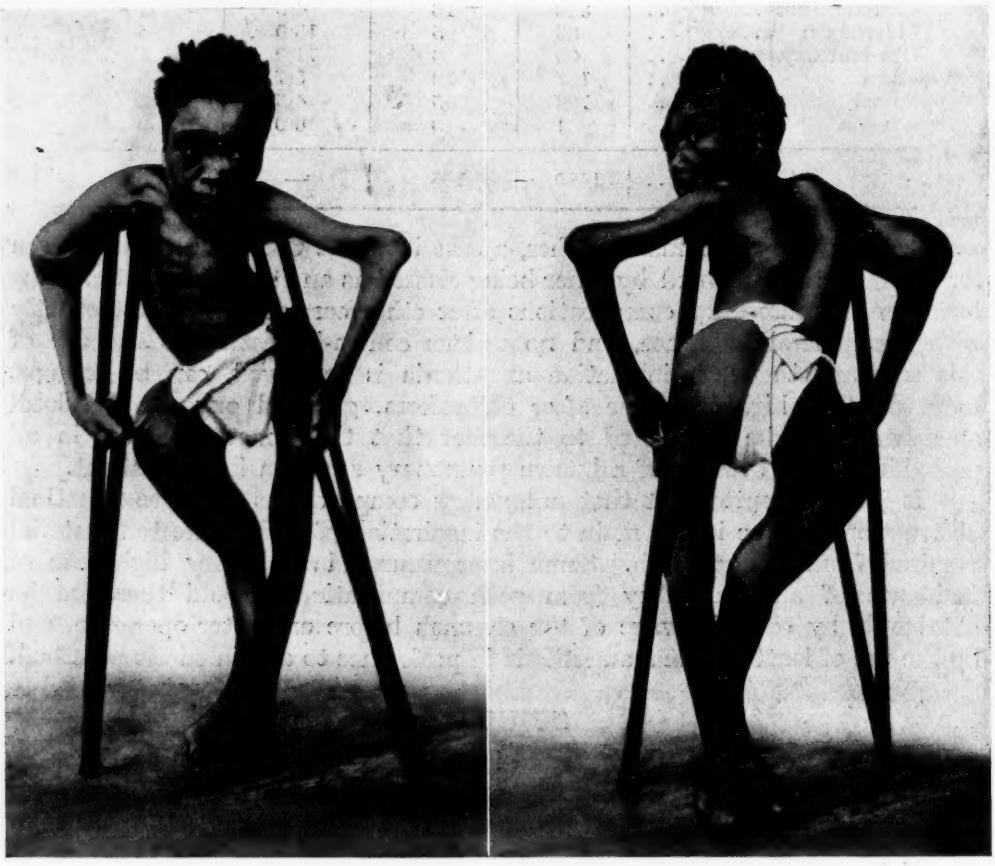

Fig. 159.—Photographs of the patient showing the condition in 1929.

Only a few radiographs were taken at that time, but cysts were found in both humeri, in the shaft of the right femur, which was fractured, the left femur, and left tibia. The skull was asymmetrical but not cystic. The

fractured femur united without incident, as did other spontaneous fractures of the left tibia and left femur during the succeeding eighteen months.

The patient was again seen in 1920 for a deformity resulting from a fracture of the right tibia and for which an osteotomy was performed. The

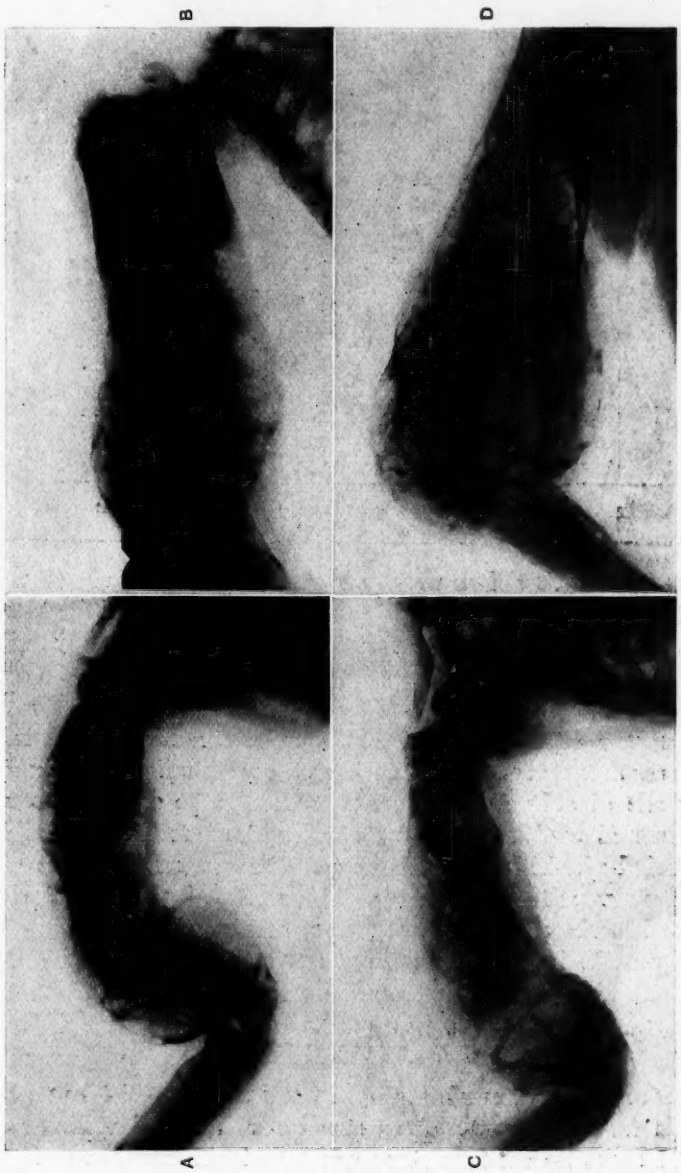

FIG. 160.—X-ray photographs of the right humerus. A, Aug. 4, 1921; B, Aug. 16, 1921, after removal of a portion of the tissue and insertion of a piece of ox-rib; C, June 14, 1922; D, Nov. 26, 1929.

notes of this period record an increased enlargement of the bones, especially of the right and left humeri, which could be dented like a celluloid ball, and were tender on deep pressure. The bones of both lower extremities were harder, did not bend on pressure, and were only slightly tender. No changes were found in the forearms, wrists, hands, feet, or ankles. The condition

of the spine and ribs was not recorded. The operation notes state that the tibia was hollowed out into a number of spaces, crossed by bony trabeculæ, in which no definite marrow or medulla could be detected, and that there

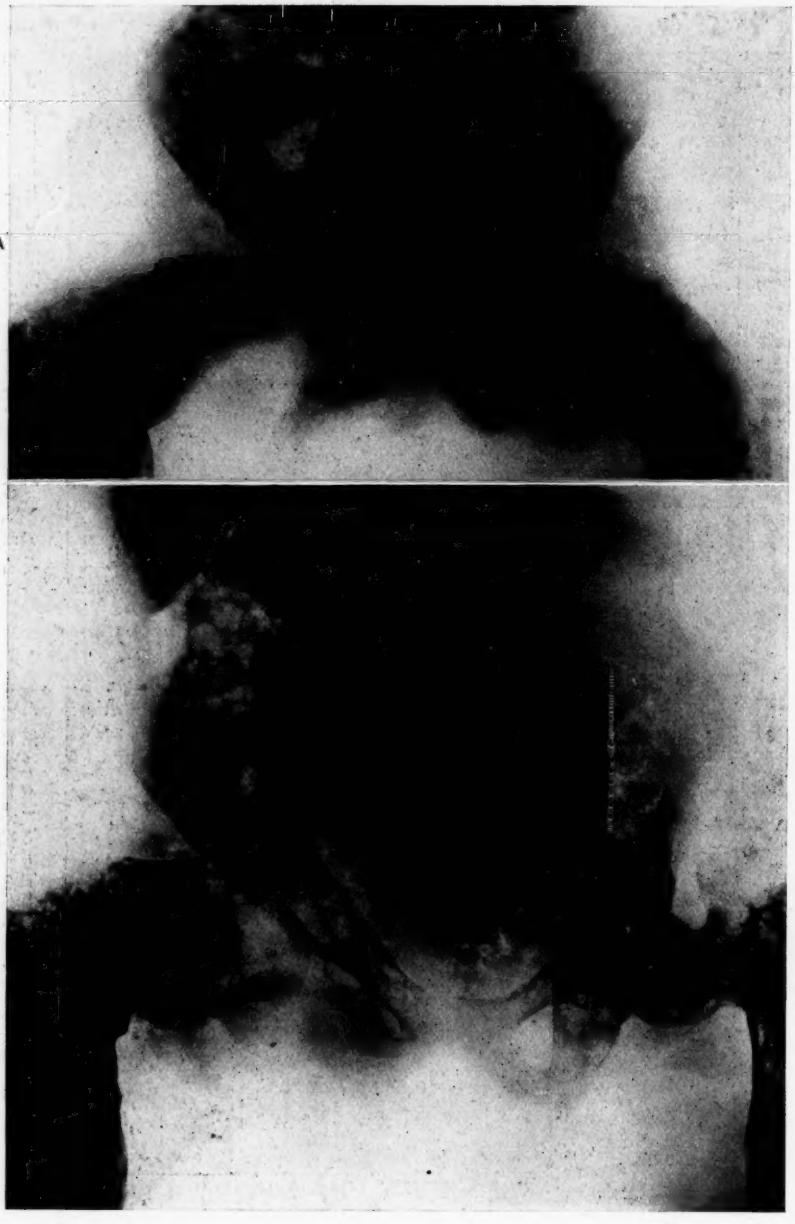

FIG. 161.—X-ray photographs of the pelvis. A, Aug. 4, 1921; B, Oct. 30, 1929.

was only a very thin layer of compact tissue. Under the microscope the removed wedge consisted mainly of bony plates enclosing a fibrovascular tissue.

FIG. 162.—X-rays of right femur. A, July 21, 1922; B, Sept. 28, 1929.

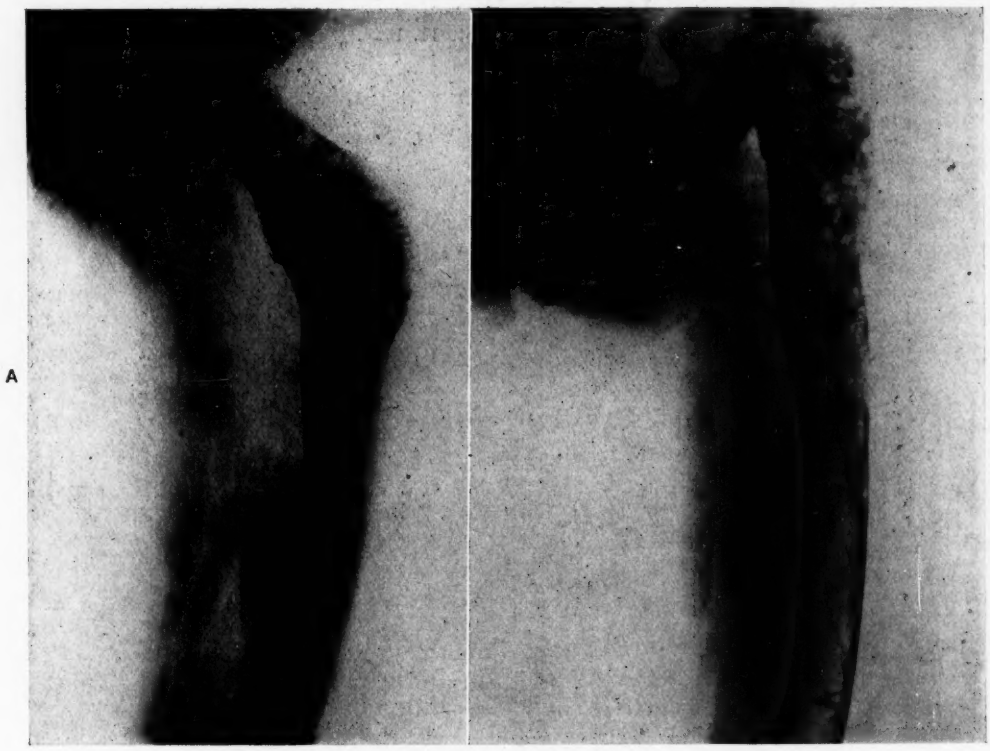

FIG. 163.—X-rays of left femur. A, Aug. 4, 1921; B, Nov. 26, 1929.

FIG. 164.—X-rays of legs. A, Right tibia and fibula, Aug. 4, 1921; B, Right and left tibia and fibula, Sept. 11, 1923.

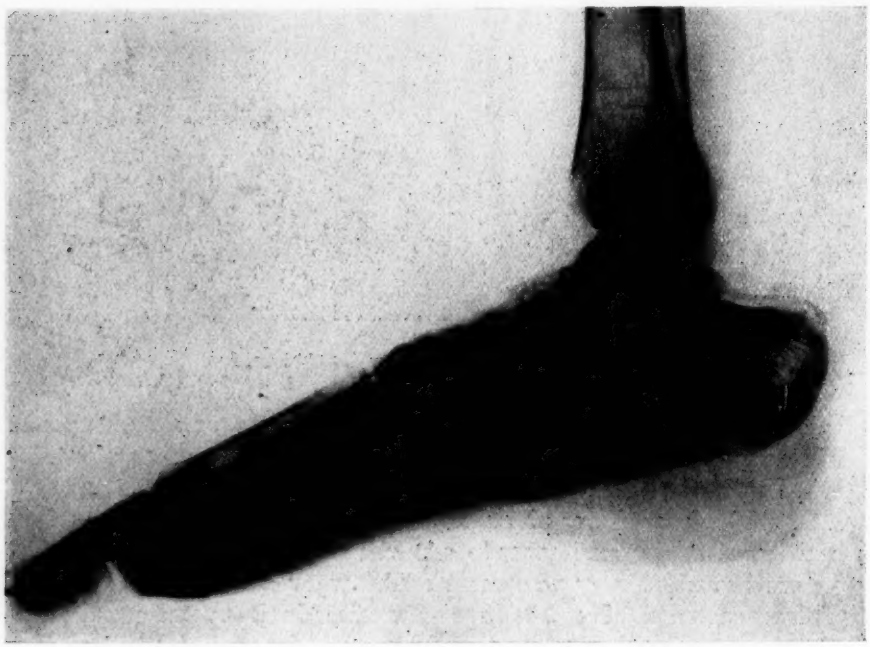

FIG. 165.—X-ray of foot showing a possible cyst in the os calcis.

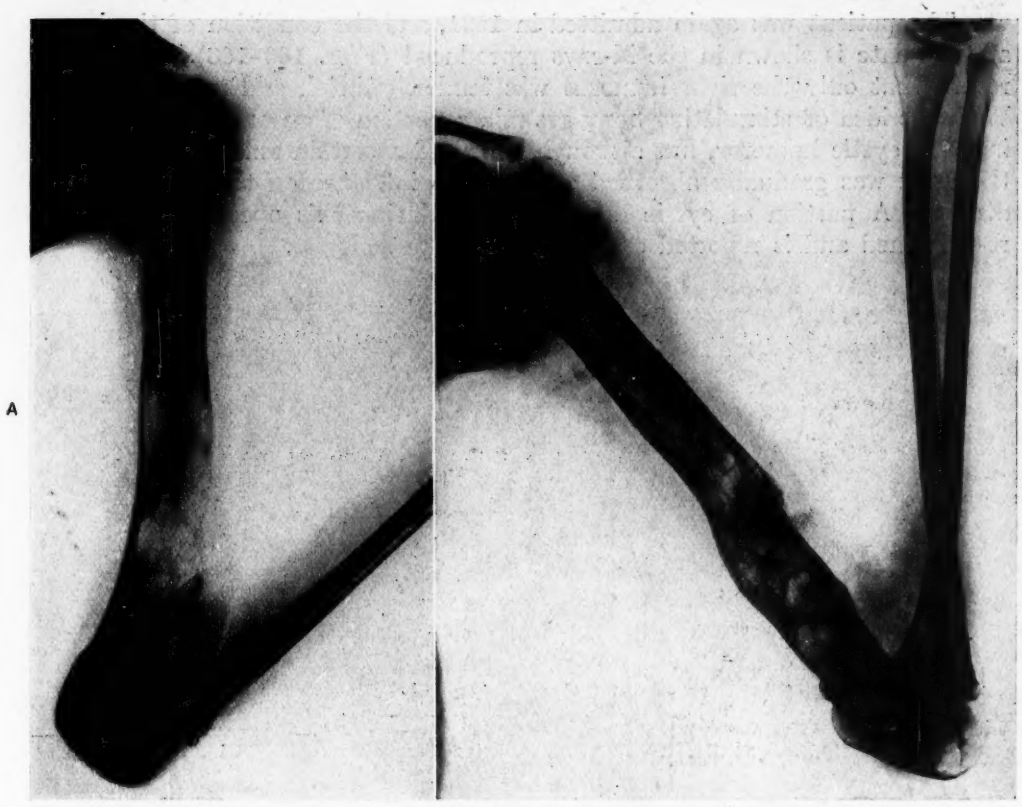

FIG. 166.—X-rays of left arm. A, Aug. 4, 1921; B, Sept. 23, 1929.

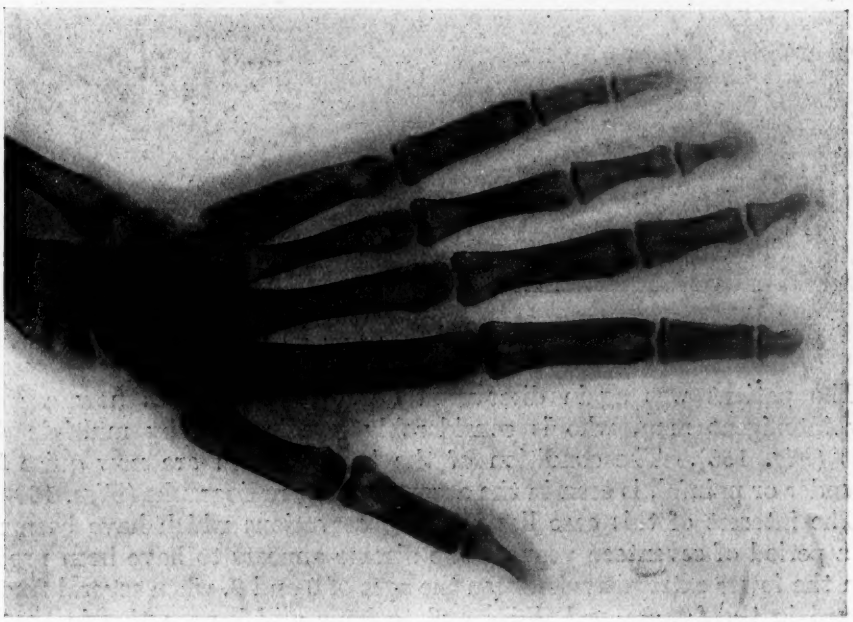

FIG. 167.—X-ray of left hand November, 1929, showing hyperostosis of the 2nd and 5th metacarpal bones and of some of the phalanges.

The patient was again admitted in 1921, and the condition of the bones at that date is shown in the X-rays reproduced (*Figs.* 160–166). The notes record that only the right humerus was tender, painful, and parchment-like. With the idea of stimulating bony growth, a portion of an ox-rib was inserted into the cystic humerus, but although it caused a certain amount of reaction, the graft was gradually absorbed and had no influence on the course of the disease. A portion of cystic bone removed during this operation has been re-examined and is reported on below by the pathologist.

FIG. 168.—X-ray of skull, Nov. 20, 1929.

The patient was again discovered during 1929, and is now a grown, fairly intelligent man, who is considerably handicapped by multiple deformities (*Fig.* 159). The condition of the bones, which are now quite hard, not tender or painful, is seen in the accompanying radiographs (*Figs.* 160–169).

The interest of this case lies in the observations which have been made over a period of seventeen years. The disease appears to have been progressing in the lower extremities between the ages of 6 and 9, when several fractures occurred in the femora and tibiæ, and to have still been active in the right

FIG. 169.—X-ray of thorax, Sept. 11, 1929.

humerus up to the age of 18. At the present time it seems reasonable to assume that the disease is no longer active, although no real attempt is being made to replace the cystic tissue by new bone formation. At no time did any pathological investigation throw light on the etiology of the condition. The Wassermann reaction has always been negative; the blood, except for a mild anæmia common in India, has been normal; and no results from careful investigation of the fæces and urine have indicated any relevant metabolic changes. The appearances in the skull remind one very much of those seen in Paget's disease, and the information obtained from the mother that birth was normal suggests that the skull deformity was due to the disease and was probably not recognized in our earlier X-rays.

FIG. 170.—Portion of bone removed from the right humerus in 1921 (*see* text).

PATHOLOGIST'S REPORT (Dr. A. Vasudevan).—Tissue from A. Boward (Sections 9401, A, B, & C, 98 and 1490). The specimen is a pale bluish cartilaginous mass roughly $3\frac{1}{2} \times 1\frac{1}{4}$ in., separated into irregular areas by strands of reddish-brown tissue, on which are seen opaque, yellowish, gritty areas of calcified material (*Fig.* 170).

Microscopical Appearances (*Figs.* 171–174).—In the main, the tissue consists of irregularly disposed tracts and islands of osteoid material embedded in a mass of vascular marrow which is in varying stages of fibrosis. The osteoid material is arranged in branching columns or islands, and does not show any Haversian canals, while lamellar arrangement is

FIG. 171.—Section of tissue from the right humerus. (Low power.) A, Columns of osteoid tissue; B, Cyst containing fibrous tissue.

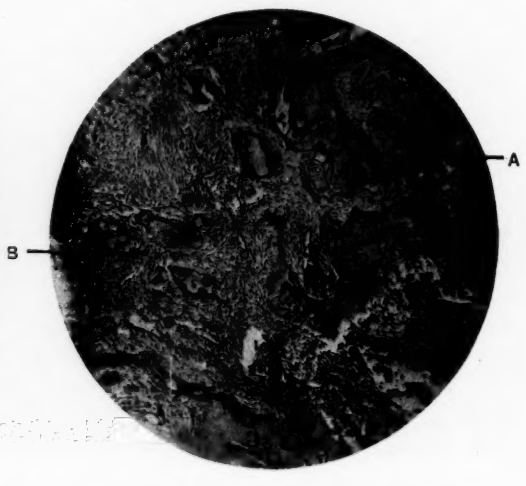

FIG. 172.—Section of tissue from the right humerus. (Low power.) A, Islands of osteoid tissue; B, Cellular fibrous tissue.

mostly absent or very faint. There are a few lacunæ in which are incarcerated cells. Most of the osteoid masses are lined externally by a definite row of darkly staining cuboidal cells (osteoblasts). In some portions this osteoid tissue is almost absent and its place is taken by large areas of degeneration, some of which show calcification. Between the masses of osteoid material is a vascular fibrous tissue in which are numerous fibroblasts, young blood-vessels,

FIG. 173.—Section of tissue from the right humerus. (High power.) Osteoid tissue showing calcification.

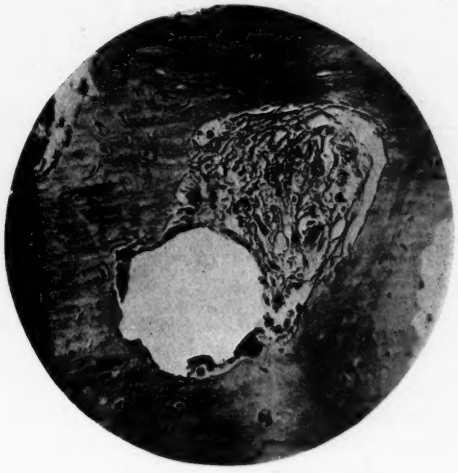

FIG. 174.—Section of tissue from the right humerus. (High power.) Cyst in bone, lined with endothelium and containing fibrous tissue.

and a few multinucleated giant cells. This is probably marrow undergoing fibrosis. This marrow tissue is scanty and is well seen in only one of the sections. Numerous cysts of varying size lined with definite flat endothelial cells, some containing blood and others coagulated eosin-staining material, are seen in the fibrous tissue. The cyst formation is not uniform, being marked in some samples of the tissue and almost absent in others.

I am very much indebted to Captain Barnard and the X-ray Institute, Madras, for the pictures which illustrate this case.

COMMENT.

(R. C. ELMSLIE.)

Further sections of the specimen removed from the humerus submitted to me by Colonel Bradfield showed nothing additional to the tissues described by Dr. Vasudevan except that considerable areas of cartilage were found.

This is a typical case of generalized fibrocystic disease in which the changes consist more in the transformation of bone into fibrous tissue and cartilage than in the formation of cysts. There seem to have been no gross cysts and no evidence of the existence of giant-cell tumours. The extreme

changes in the upper ends of the femora seem to be very characteristic of this clinical type of the disease. In one recent case in which the pathological picture was similar to that described by Colonel Bradfield, investigation showed that the blood calcium and phosphorus were within normal limits, and exploratory operation failed to disclose any parathyroid tumour. Parathyroid tumours have been found in most of the cases in which there is extensive cystic formation. It may be that the fibrosing form is a different disease, or it may be that it represents a late and inactive stage.

Colonel Bradfield's case is of very great interest because it illustrates the progress of the disease over a long period.

REFERENCE.

[1] ELMSLIE, R. C., *Brit. Jour. Surg.*, 1914, ii, 17.

HYPERPARATHYROIDISM: GENERALIZED OSTEITIS FIBROSA.*

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WITH OBSERVATIONS UPON THE BONES, THE PARATHYROID TUMOURS, AND NORMAL PARATHYROID GLANDS.

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THE purpose of this paper is to set forth the evidence upon which is based the view that generalized osteitis fibrosa (von Recklinghausen) is a disease of endocrine origin. According to this view the changes in the bones are due to hyperparathyroidism, a condition associated with hyperfunction of a parathyroid tumour. Four such cases are described, and in three the effects of removal of a parathyroid tumour are recorded. Four cases of focal osteitis fibrosa are described in order to place on record the absence of any evidence of hyperparathyroidism in this disease. Finally, a case of osteomalacia is recorded. Here the blood chemistry, metabolism, and histology suffice to show that osteomalacia and generalized osteitis fibrosa are unrelated diseases.

EFFECTS OF THE PARATHYROID HORMONE.

The parathyroid glands exert a specific effect upon calcium metabolism. The pioneer work of MacCallum and Voegtlin (1909) demonstrating a reduction of serum calcium in dogs after parathyroidectomy has been abundantly confirmed. It is well established that this condition is relieved by the administration of calcium salts. The idea that it is due to guanidine intoxication remains unsupported by adequate evidence.

Since the isolation by Hanson (1924) and Collip (1925) of the active principle of the parathyroid gland (parathormone) it has been repeatedly demonstrated that the injection of the extract causes an elevation of the serum calcium. Brehme and György (1927) found that parathormone lowers the blood phosphorus and shifts the pH of the blood towards the acid side without affecting the CO_2 combining power of the blood. Reiss (1928) and Aub (1928) found independently that parathormone lowers the level of the blood phosphorus. This appears to be the first action, the elevation of serum calcium following only after a long latent period. Whether the effect on phosphorus is the primary effect of parathormone remains for further work

Being the basis of an Arris and Gale Lecture delivered before the Royal College of Surgeons, in London, on January 30th, 1931. Received for publication May 12th, 1931.

to establish. However, the dramatic effect of parathormone is the marked elevation of serum calcium.

The study of the influence of parathormone on the excretion of calcium and phosphorus has demonstrated less striking results than would have been expected from its effect upon the blood. In normal individuals a constant dose of parathormone causes the phosphorus excretion to rise abruptly to a maximum in the first three-day period, while the maximal increase of the calcium excretion follows more gradually. After discontinuing parathormone the phosphorus excretion falls to normal more abruptly than does the calcium (Albright, Bauer, Ropes, and Aub, 1929). This early rapid excretion of phosphorus may account for the primary fall in the plasma phosphorus and is further suggestive evidence of the contention of Greenwald (1924) of the primary influence of phosphorus in regard to tetany.

Parathormone raises the serum calcium in normal persons. There is great individual variation in this response. A dose of 50 units of parathormone daily is usually found to have little influence on the level of the serum calcium, yet it approximately doubles the excretion of calcium and phosphorus. When 100 units a day are given to normal individuals the serum calcium level is raised to an average of 12·5 mgrm. per 100 c.c., and there is an average rise in the urinary calcium excretion to six times the normal level. The source of such large amounts of calcium salts appearing in the urine is of fundamental importance. The evidence available both in animals (Greenwald and Gross, 1925) and in man (Hunter and Aub, 1926) points to the conclusion that *these calcium salts are derived from the bones.*

Effects of Over-dosage with Parathyroid Extract.—The work of Collip on dogs (1925) brought to light a new entity—hypercalcæmia. This condition has since been found to occur in man, both spontaneously and as the result of parathyroid over-dosage. In Collip's observations on dogs no ill-effects were noted if the dosage of parathyroid extract was only sufficient to cause a rise in the serum calcium to 14 or 15 mgrm. per 100 c.c. Large doses of the hormone, however, administered five times in the twenty-four hours often caused death within forty-eight hours of the first dose. Though in such cases the serum calcium rose to 20 or 21 mgrm. per 100 c.c., Collip made no claim that the hypercalcæmia was the immediate cause of death. In describing the condition of these animals he states that "the clinical manifestations of hypercalcæmia in dogs appear to be loss of appetite, dullness, drowsiness verging on coma, general atonia, and a failing circulation. The animals are also obviously dehydrated, the blood becomes very concentrated, and it becomes a matter of great difficulty to secure serum from blood samples for analysis even when a high power centrifuge is used. Immediately after death the blood in the heart and great vessels forms a firm clot." Complete investigations of the blood chemistry showed that the inorganic phosphorus rose in the later stages of hypercalcæmia and that there was nitrogen retention. Thus in one dog the blood at death had a phosphorus content of 13 mgrm. per 100 c.c. and a urea content of 111 mgrm.

During our investigations a severe hypercalcæmia was produced in one case by over-dosage with parathormone (Hunter and Aub, 1926). The patient was a man of 60 years suffering from chronic lead poisoning. Parathormone

had been given in increasing doses for seven days, the total amount being 365 units. On the seventh day the serum calcium had risen to 19·8 mgrm. per 100 c.c. It remained at this level for forty-eight hours; then, though all treatment had been discontinued, it fell only very gradually to normal levels during the next three days. The plasma phosphorus dropped to 2·7 mgrm. per 100 c.c., but later it rose to 6 mgrm. per 100 c.c., and this occurred twenty-four hours after the maximum rise in calcium. The non-protein nitrogen showed a rise to a maximum of 95 mgrm. per 100 c.c., this rise occurring two days after the maximum rise in calcium. During the next week it fell gradually to within normal limits. The changes in the physical properties of the blood observed by Collip in dogs suffering from parathyroid over-dosage were absent. Throughout the whole time the patient remained up and about, and, except for slight nausea and loss of appetite, appeared to be normal.

Prolonged over-dosage with parathormone in the dog may give rise to metastatic calcification in the kidneys, lungs, myocardium, and gastro-intestinal tract (Hueper, 1927). It is of interest to note that under certain biological conditions hypercalcæmia may occur as a normal phenomenon. It has been shown that the serum calcium of certain birds increases very considerably at the period of ovulation. Thus in the female pigeon the rise in the serum calcium begins 123 hours before the formation of the egg-shell. Subsequently, during a period of from three to five days these birds will stand, without trace of adverse effect, a hypercalcæmia up to 20 mgrm. per 100 c.c. (Riddle and Reinhart, 1926). Similarly the female cod in the spawning season has a blood calcium varying from 12·7 to 29 mgrm. per 100 c.c., whereas the corresponding figure in the male lies between 9 and 12·5 mgrm. (Hess, Bills, Weinstock, and Rivkin, 1927). This calcium is probably required for the elaboration of the eggs, which are especially rich in that element.

GENERALIZED OSTEITIS FIBROSA OF VON RECKLINGHAUSEN.

Generalized osteitis fibrosa is a disease which progresses with pain, fractures, and disabling deformities, and is usually fatal. There is widespread pathological resorption affecting all the bones. In addition there are multiple foci of osteitis fibrosa with or without benign giant-celled tumours and cysts. It is a disease entity which I believe to be distinctly different from focal osteitis fibrosa. In the latter there may be one or more focal lesions, the essential point being that outside these lesions all bony tissue is normal.

In a Festschrift written in 1891 in honour of the seventy-first birthday of Virchow, von Recklinghausen gave the first accurate description of the disease entity which now goes by his name. His contribution to the Festschrift is very involved, for he describes more than one bone disease. There can be no doubt, however, that his Cases 5 and 7 constitute the discovery of generalized osteitis fibrosa. It is important for us to notice that he went to the trouble of describing two cases of puerperal osteomalacia (Cases 8 and 10) in order to place on record that "so many facts differentiate Case 7 from true osteomalacia". He describes his Case 7 as "osteitis fibrosa with marked bone softening and multiple osteosarcomata". The patient was

a man of 40, thought to be suffering from osteomalacia. There was a history of eighteen months' bone pain with bowing of the bones and multiple spontaneous fractures. At necropsy the bones were soft and deformed so that with a saw they cut like rotten wood, and the shafts could be cut with a knife using moderate force. All the bones in the skeleton were affected, and seemed histologically to be formed of a tough connective tissue. Brown-red projecting tumours were found in the fibula, iliac crest, and upper and lower jaws.

In our subsequent knowledge of this disease there is ample clinical and pathological evidence to establish the benign nature of these giant-celled tumours. The cells themselves are similar to the osteoclasts normally present in Howship's lacunæ.

Thirteen years after von Recklinghausen first described generalized osteitis fibrosa an important step was made towards solving the problem of its etiology. This was a description by Askanazy in 1904 of a case of generalized osteitis fibrosa associated with a parathyroid tumour. The patient was a woman of 51, complaining of pains in the limbs, and suffering from multiple spontaneous fractures. At necropsy, to the left of the left thyroid lobe there was a tumour which looked almost like a second left thyroid lobe. A parathyroid origin of this tumour was suspected. The femur was fractured in three places, and all the bones of the skeleton cut easily with a knife. Microscopically the process of destruction of old bone was carried out by numerous osteoclasts lying in Howship's lacunæ. Sometimes small bony particles were seen surrounded by osteoclasts, and occasionally these cells alone were seen, singly or in groups, free in connective tissue.

Since its significance was scarcely suspected, the parathyroid tumour mentioned by Askanazy in this case passed unnoticed. However, the description by Erdheim in 1907 of three cases of osteomalacia associated with parathyroid enlargement called forth many other observations of bone disease associated with hyperplasia or tumour formation in the parathyroid glands.

In 1925 Hoffheinz, rejecting all cases where the parathyroid enlargement was indefinite or inadequately described, collected from the literature 45 cases with *measurable* enlargement of one or more parathyroid glands. Of these, 27 were associated with definite bone disease, including 17 of generalized osteitis fibrosa, 8 of osteomalacia, and 2 of rickets. He quoted increases of size up to $7 \times 2{\cdot}5 \times 1$ cm. The histological changes were either those of hyperplasia or of adenoma, and it is important to notice that sometimes more than one parathyroid gland was affected.

In cases of generalized osteitis fibrosa renal calculi have commonly been observed, and areas of metastatic calcification have been found in the lungs, stomach, kidneys, and myocardium (Dawson and Struthers, 1923).

Relation of Parathyroid Tumour to Changes in Bone.—Amongst pathologists a difference of opinion arose as to whether the parathyroid tumour was primary or secondary in relation to the bone disease. Erdheim himself defended the view that the disease of the skeleton was the primary factor, and that skeletal decalcification created such a demand for calcium that a compensatory hypertrophy of the parathyroid glands occurred. Anatomical evidence against this view was found in the fact that, in generalized osteitis fibrosa, hypertrophy or tumour formation was often confined to one

parathyroid gland, the others remaining apparently normal. On account of Erdheim's investigations the whole question was repeatedly discussed at scientific meetings in Vienna. As early as 1915 Schlagenhaufer at such a meeting raised the question whether it was not justifiable to attempt the extirpation of a parathyroid tumour in cases of generalized osteitis fibrosa. Maresch supported this suggestion, but it was not until 1926 that Mandl, of the Vienna school, first performed this operation. In view of the Vienna controversy, it is of great interest that he decided to explore the neck only after treatment by parathyroid transplants and parathyroid tablets had failed to relieve the symptoms. The patient was a man of 38 with a history of pains in the pelvis and lower extremities for five years. Radiograms showed osteitis fibrosa of femora, pelvis, tibia, and ischium. Spontaneous fracture of the femur occurred, and he became unable to stand or sit. Four parathyroid bodies from an accident case were transplanted into the abdominal wall. No improvement occurred. It was therefore decided to explore the neck, though no tumour could be felt. A parathyroid tumour (2·5 × 1·5 × 1·2 cm.) was removed at operation. Pains in the bones disappeared a few days after operation. The urinary calcium excretion dropped to one-eighth of the pre-operative value. Three and a half years after the operation he still had no pains in the bones, and walked with a stick. The serum calcium at that time is reported as 13 to 14 mgrm. per 100 c.c., and no increase in density of the X-ray shadows of the bones had occurred.

HYPERPARATHYROIDISM.

We now turn to the biochemical aspect of this problem. In 1926 Hannon, Shorr, McClellan, and Du Bois investigated the case of a man of 34 with the symptoms and signs of a generalized disease of the skeleton. Radiograms showed an extensive decrease in the density of the shadows of bones, and a large cyst in the right femur. There was a high blood calcium (serum Ca 15·3 mgrm. per 100 c.c.) and a low blood phosphorus (plasma inorganic P 1·4 mgrm. per 100 c.c.). In 1929 Richardson, Aub, and Bauer investigated the same case, and found that the urinary output of calcium and phosphorus on a low calcium diet was six to seven times greater than was found in normal individuals under identical conditions. They found that these changes in metabolism were equivalent to those of a normal individual receiving 100 units of parathormone daily. It was, therefore, reasonable to suppose that this patient was suffering from hyperparathyroidism. Exploration of the neck revealed no tumour, but this does not mean that no such tumour existed, for we now know that parathyroid tumours may be deeply situated behind the trachea or even in the mediastinum. It was the study of this case and the use of Aub's methods which led to the discovery of many cases of hyperparathyroidism in the United States and in this country. Meanwhile in Germany, Austria, Holland, and France the work of Mandl was producing the same effect.

ABSTRACTS OF PUBLISHED CASES.

MANDL (Vienna, 1926).—Male, 38. Osteitis fibrosa of pelvis and both femora. Totally disabled by pain. Serum Ca 18·2 mgrm. Increased urinary excretion of

Ca. Parathyroid adenoma removed (2·5 × 1·5 × 1·2 cm.). Urinary Ca excretion dropped to one-eighth the pre-operative value. Three and a half years later no pain. Walks with a stick. Has gained 16 kilos. Serum Ca 13 to 14 mgrm. No increase in density of X-ray shadows of bones.

LAMBIE (Edinburgh, 1927).—Female, 30. Generalized osteitis fibrosa. Serum Ca 17 mgrm., and inorganic P 2·7 mgrm. On a milk diet Ca output in urine normal, but considerable increase in fæces. No operation. Diagnosis confirmed at post-mortem, and adenoma of parathyroid found.

GOLD (Vienna, 1928).—Female, 54. Osteitis fibrosa generalisata (von Recklinghausen) with cysts in right humerus and in three ribs. Mal-union of fracture of left femur. Serum Ca 13·1 mgrm. Increased Ca excretion in urine. Parathyroid adenoma (2·5 × 1·5 cm.) removed. Serum Ca fell to 9·9 mgrm. one month after operation. Five months later much less pain, serum Ca 9·6 mgrm. Positive Ca balance. No increase in density of X-ray shadows of bones.

BARRENSCHEEN and GOLD (Vienna, 1928).—Sex and age not stated. Osteitis fibrosa cystica generalisata Recklinghausen. Pain in the bones. Serum Ca 14·2 mgrm. Slight increase of urinary Ca excretion. Removal of histologically normal parathyroid gland caused no clinical improvement. Two months later patient rather worse. Serum Ca 16·0 mgrm.

DUKEN (Jena, 1928). *Case* 1.—Female, 7. Osteodystrophia fibrosa. Pains in legs, tumour of frontal bone, protrusion of left eye. Tumour of 2 cm. diameter in left side of neck thought to be enlarged parathyroid. Serum Ca 14 mgrm., and inorganic P 5 mgrm. No operation. (Post-mortem report unsatisfactory and incomplete.)

Case 2.—Female, 14. Osteodystrophia fibrosa with late rickets. Ceased to grow at 12. Genu valgum. Hypotonicity of muscles. Polyuria. Fairly clear swelling in the neck (size and shape not stated). Serum Ca 20·8 mgrm. and inorganic P 3 mgrm. Resection of maxilla for tumour—histological examination showed osteitis fibrosa. No operation on neck.

BECK (Kiel, 1928).—Female, 41. Generalized osteitis fibrosa. Amputation of leg for supposed sarcoma. Three years later fell and fractured femur. True nature of condition then recognized clinically, confirmed by X rays, and proved histologically. Six years after the fracture Ca and P levels in blood raised (no figures given). Urinary Ca excretion three times the normal. Two parathyroid tumours, size of almond and coffee bean, removed. Three days after operation Ca and P values in blood normal, and Ca excretion in urine approximately normal. Tetany on fifth day, accompanied by a psychosis. Died of exhaustion on twentieth day.

RICHARDSON, AUB, and BAUER (Boston, 1929); HANNON, SHORR, MCCLELLAN, and DU BOIS (New York, 1930).—Male, 30. Generalized disease of bones with extensive areas of decalcification and a large cyst in the right femur. Serum Ca 15·3 mgrm., and inorganic P 2·1 mgrm. Great increase in urinary Ca excretion. Exploratory operation on neck. No tumour found. Removal of two normal parathyroid glands. Two years after operation, considerable symptomatic improvement. Serum Ca 13·9 mgrm., and inorganic P 2·6 mgrm.

BARR, BULGER, and DIXON (St. Louis, 1929).—Female, 56. Osteitis fibrosa with benign giant-celled tumours of phalanx and ulna. Spontaneous fracture of clavicle. Hypotonia of muscles and joints. Increased frequency of micturition. Bilateral renal calculi. Serum Ca 16 mgrm., and inorganic P 1·4 mgrm. Great increase in urinary Ca excretion. Globular mass size of a small walnut felt embedded in left lobe of thyroid gland. Parathyroid adenoma removed (no measurements given). Severe tetany two days after operation. Calcium balance became positive. Swelling in superior maxilla became smaller.

WILDER (Rochester, Minn., 1929, 1931).—Female, 35. Generalized osteitis fibrosa with giant-celled tumours of inferior maxilla and femur. Six years, pain in hip ultimately affecting all bones. Serum Ca 13·2 mgrm., and inorganic P 1·9

mgrm. Spherical mass palpable in neck: malignant adenoma of parathyroid gland removed (5 × 3·5 × 3 cm.). Three days later tingling in fingers and toes, but no tetany; serum Ca 7·1 mgrm. Great improvement, gave up crutches. Four months later serum Ca 8·3 mgrm., and inorganic P 1·8 mgrm., increased density of X-ray shadows of bones. Eighteen months after operation some pain in bones of hands, feet, and shoulders. Serum Ca and plasma P normal. X-ray shadows of bones still far from normal density, no cysts.

Boyd, Milgram, and Stearns (Iowa City, 1929).—Male, 19. Generalized osteitis fibrosa. Progressive bowing of legs. Thirst and polyuria. Serum Ca 17·6 mgrm., and inorganic P 2·2 mgrm. Urinary Ca output three times the normal. Parathyroid adenoma removed (3·5 × 2·5 cm.). Chvostek sign appeared day after operation with serum Ca 12·3 mgrm. Trembling of extremities with serum Ca 5·0 mgrm., but no tetany. Polydipsia, polyuria, and pains in limbs disappeared. After ten days calcium balance positive. Three months after operation blood Ca and P normal; bones showed evidence of progressive repair.

Snapper (Amsterdam, 1929).—Male, 56. Osteitis fibrosa generalisata (von Recklinghausen) with cysts in scapula and metatarsal. Totally disabled by severe pains in bones. Spontaneous fracture of femur. Under observation four years, during which time density of X-ray shadows of bones decreased. Serum Ca 23·6 mgrm., and inorganic P 2·1 mgrm. Greatly increased Ca and P excretion in urine. Tumour palpable in neck: parathyroid adenoma removed (2·5 × 1·5 cm.). Day after operation pains ceased. Tremor, acute mania, Chvostek sign with serum Ca 6·6 mgrm. Ca excretion in urine fell to normal. Four months later great clinical improvement, serum Ca 10·6 mgrm. and inorganic P 3·3 mgrm. Fracture healed, and after five months X-ray shadows of bones were more dense. Able to walk after eight months.

Eggers (quoted by Mandl, 1929).—Female (age not stated). Generalized osteitis fibrosa. Serum Ca 14·6 mgrm. Parathyroid tumour size of hazel nut removed. Serum Ca reduced to 5·7 mgrm. Definite clinical improvement. Death by accident. Post-mortem confirmed diagnosis.

Hunter (London, 1929, 1930, *Case* 4).—Female, 41. Generalized osteitis fibrosa. Three years, pain in back and left thigh. Four months, walked with sticks. Spontaneous fracture of neck of femur. Tenderness on pressure upon bones. No swelling palpable in neck. Radiograms showed greatly diminished density of shadows of bones. Serum Ca 16·7 mgrm. and inorganic P 1·0 mgrm. Plasma phosphatase 1·9 mgrm. Ca output in urine six times the normal. Cystic parathyroid tumour removed (3·7 × 3·0 × 3·0 cm.). Histology of tumour: hyperplasia of parathyroid gland. Histology of bone: generalized osteitis fibrosa. Two days after operation serum Ca 9·1 mgrm. Latent tetany only. On fourth day bones no longer tender to pressure. Ca output in urine fell approximately to normal. Eight months after operation she walked in a caliper splint, and seven months later unaided. No further pains in bones. Seventeen months after operation she had gained 2 st. 6 lb. in weight. Serum Ca and inorganic P remained normal. Plasma phosphatase remained high. In controlled radiograms density of bone shadows had increased slightly, but was not nearly normal.

Barr and Bulger (St. Louis, 1930, *Case* 2).—Male, 38. Multiple giant-celled tumours of bone, localized to upper and lower jaws. No obvious decalcification or osteomalacia of other bones. Hypercalcæmia up to 16·7 mgrm. Inorganic P as low as 1·2 mgrm. Negative calcium balance. Tumour palpable just above inner end of left clavicle, especially when swallowing. Parathyroid tumour removed; twice as large as was expected from palpation. Part of it was re-implanted in the rectus sheath. In twenty hours the serum Ca dropped to 10·6 mgrm. and reached its minimum ten days after operation at a level of 8·3 mgrm. Urinary output of Ca decreased. Ca balance became positive. No tetany occurred. Two months after operation quite well. Weight increased. Serum Ca 10·5 mgrm. Inorganic P 2·9 mgrm. X-ray examination showed no progress of bone disease. The case had been treated earlier with X rays because of a diagnosis of malignant tumours of bone.

ASK-UPMARK (Lund, 1930).—Male, 46. Osteitis fibrosa generalisata (Engel-Recklinghausen). Twelve months, pain in feet, knees, and hips, later becoming very severe. Spontaneous fractures in femur and humeri. Great wasting. Radiograms of bones showed general decalcification. Serum Ca 10·0 mgrm. At autopsy only one parathyroid gland identified, this being more than four times normal size.

BALL (Rochester, Minn., 1930).—Male, 50. Generalized osteitis fibrosa. Seven years, pain in dorsa of feet, later affecting knees, lumbar spine, right hand, and wrists. Four attacks of ureteric colic with passage of gravel on one occasion. Spontaneous fracture of 1st lumbar vertebra. Epigastric pain, anorexia, and mild nausea. Kyphosis. Nodule palpable in lower pole of right lobe of thyroid gland. Hypotonia of muscles. Radiograms of bones showed multiple areas of absorption. Serum Ca 15·4 mgrm. Inorganic P 1·7 mgrm. Plasma phosphatase increased. Negative calcium balance. Double resection of thyroid gland. Cystic colloidal and fœtal adenoma. No parathyroid tissue found. After operation serum Ca remained high and inorganic P low. Excretion of calcium remained above normal level.

COMPERE (Chicago, 1930).—Female, 59. Generalized osteoporosis with no sign of bone cysts or tumours. Five years, pain in bones of legs, particularly feet. Two and a half years, bowing of both legs and general weakness. Hypotonicity of muscles. Spherical nodule, 2 cm. in diameter, palpable in lower pole of right lobe of thyroid gland. Serum Ca 12·6 mgrm. Inorganic P 3·7 mgrm. Increased urinary output of calcium. At operation nodule when excised proved to be thyroid adenoma. Parathyroid adenoma (1·0 × 1·8 cm.) removed from behind lower pole of left lobe of thyroid gland. Normal left upper parathyroid body also removed. Developed tinglings in fingers and numbness in hands. No tetany. Serum Ca fell to 6·9 mgrm. after two days, but after two months was 11·1 mgrm. Urinary Ca output reduced to one-fifth of pre-operative level. No change in radiograms of bones after five months. General symptomatic improvement with gain in weight.

PEMBERTON and GEDDIE (Rochester, Minn., 1930).—Female, 14. Generalized osteitis fibrosa. Sixteen months, progressive weakness, loss of weight, vomiting, polydipsia, polyuria. Hypotonia of muscles. Radiograms showed diffuse decalcification of bones but no loss of normal structure. Serum Ca 16·3 mgrm. Inorganic P 2·5 mgrm. Negative Ca balance. No tumour palpable in neck. Adenoma of parathyroid gland removed (1·5 × 1·3 × 1·3 cm.). After operation gastro-intestinal and other symptoms rapidly improved. Serum Ca 7·6 mgrm. Inorganic P 3·9 mgrm.

LÉRI, LAYANI, LIÈVRE, and WEILL (Paris, 1930).—Male, 31. Osteitis fibrosa of von Recklinghausen. Five years, pains in right leg. Four years, attack of renal colic. Three years, pain on walking, swellings in tibiæ and left ulna. Two years, pain in left hip, spontaneous fracture of left femur. Swellings and tender areas in bones. Radiograms showed diffuse decalcification of skeleton with cyst formation. Serum Ca 19·8 mgrm. Histological section of ulna showed osteitis fibrosa with giant cells. Later, other spontaneous fractures causing severe skeletal deformity. Further attack of renal colic. Parathyroid tumour size of small bean removed. Histology: adenomatous hyperplasia. Tetany on tenth day. Great improvement. Sixteen months after operation: gained weight, walked with sticks, serum Ca 12·7 mgrm. Increased density of X-ray shadows of bones, with decrease in size of cystic areas.

FRASER (London, 1930). *Case* 1.—Female, 42. Generalized osteitis fibrosa with cysts of bone. Ten years, pain in bones. Spontaneous fractures of both humeri. Many cysts in long bones curetted. Radiograms showed decreased density of shadows of bones with cyst formation. No renal calculi seen. Serum Ca 14·6 mgrm. Parathyroid adenoma removed. Serum Ca day after operation, 5·9 mgrm. Pains in bones disappeared. Able to walk a mile. Seven months later returned with pains in arms and thighs; serum Ca 8·2 mgrm.

Case 2.—Female, 26. Diffuse osteitis fibrosa. Three years, pain in bones. Admitted with spontaneous fracture of left femur. Radiograms showed generalized changes in bones; small renal calculi in both kidneys. Serum Ca 16·4 mgrm.

Cystic adenoma of parathyroid gland removed. Serum Ca day after operation, 7·5 mgrm. Fracture united. Three months after operation: pains in bones still present; unable to walk without assistance; no increase in density of X-ray shadows of bones; serum Ca 9·6 mgrm.

Case 3.—Female, 23. Fibrocystic disease of bones. History of fall when aged 14, followed three years later by swellings of terminal phalanges of fingers and of wrists. Cysts curetted: sections showed osteitis fibrosa with cyst formation. Marked deformity of hands, long bones, pelvis, and skull. Large bilateral renal calculi. Serum Ca varied between 12·0 and 15·2 mgrm. Parathyroid tumour removed. Day following operation, serum Ca 7·3 mgrm.

WENDEL (Magdeburg, 1930, *Case* 2).—Female, 17. Generalized osteitis fibrosa. Two years, had to give up sports because of sacral backache. Twelve months, fracture of left femur, shortly followed by fracture of right femur. Radiograms showed multiple foci of osteitis fibrosa, especially in both femora, humeri, and spine. Serum Ca varied between 15 and 18·9 mgrm. Head of left fibula explored; histological section showed benign giant-celled tumour. At operation left lower and right upper parathyroid glands noticeably enlarged (no measurements given). Left lower parathyroid gland removed and found histologically normal. After operation serum Ca remained high.

ROSENBACH and DISQUÉ (Potsdam, 1930).—Female, 24. Generalized osteitis fibrosa. Severe thirst and polyuria suggesting diabetes insipidus. Pains in head, back, and limbs, loss of weight, muscular weakness, vomiting, loss of appetite. Spontaneous fractures of left femur and right humerus. Radiograms showed severe generalized osteitis fibrosa. (Blood chemistry not recorded.) Great increase in urinary Ca excretion. Soft grey tumour of right inferior parathyroid gland removed (no measurements given). Histology: adenoma or hyperplasia. After operation vomiting abruptly ceased and appetite returned. Oliguria. Urinary Ca output fell to one-fifth of pre-operative level. Walked with aid of sticks.

HURST and COSIN (London, 1931).—Male, 17. Generalized osteitis fibrosa. Three years, genu valgum. Spontaneous fracture of left femur. Large swellings in each thigh. Two years, noticed small tumour in neck. Severe deformities of bones with tenderness on pressure. Firm oval tumour felt deeply situated in neck on left side of trachea. Excess of dark hair on pubes, abdomen, and back. Radiograms: greatly diminished density of all bones; trabeculated cysts in both femora with pathological fractures. Bilateral renal calculi. Serum Ca 16·5 mgrm. Inorganic P 2·1 mgrm. Plasma phosphatase increased. Urinary calcium output increased. Cystic adenoma (2·7 × 2·2 × 2·0 cm.) of parathyroid gland removed from behind upper pole of left lobe of thyroid gland. Tingling of fingers day after operation. On third day Chvostek and Trousseau signs positive. Fifth day, serum Ca 7·8 mgrm., inorganic P 3·9 mgrm.

QUICK and HUNSBERGER (Philadelphia, 1931).—Male, 25. Five years, polydipsia, polyuria. Pains in back, arms, and legs. Persistent nausea. Four years, spontaneous fracture of femur, followed by other fractures. Swelling in lower end of left radius explored; histological section showed giant-celled tumour. Three years, deformities progressed, multiple swellings appeared in various bones. Hæmaturia. No renal colic. One year, extreme deformity of all bones except those of head, hands, and feet. Diminution of 25 in. in total height. Radiograms showed marked decalcification of all bones, with innumerable fractures, and evidence of tumours and cysts. Discrete dense shadows in region of left kidney. Serum Ca 15·7 mgrm., and inorganic P 2·7 mgrm. Plasma phosphatase increased from four- to five-fold. Fullness in left side of neck suggestive of a tumour. At operation parathyroid tumour (1·7 × 1·5 × 1·1 cm.) removed from deep surface of left lobe of thyroid gland. Histological picture: hyperplasia. In one week serum Ca fell to 11·5 mgrm., but in three months had risen again to 15 mgrm. At second operation, three months after first, further portion of tumour (3·5 × 2·0 × 1·5 cm.) removed. Twenty-four hours later, serum Ca 8·9 mgrm. Tetany on fourth day relieved by calcium gluconate and calcium chloride given intravenously. No tetany after

thirteenth day. Estimation of Ca balance showed an increased positive balance compared to the figure obtained before operation. Radiograms taken one month after second operation showed increased density of shadows of bones.

SNAPPER and BOEVE (Rotterdam, 1931, *Case* 2).—Female, 35. Three years, swelling of right heel, radiograms showed cyst in calcaneus. Two years, swelling in right tibia explored; histological section showed giant-celled tumour. Four months, pain in right thigh, spontaneous fracture of right femur which remained un-united. Radiograms showed poor bone shadows with cysts in ilium and femora. No tumour felt in neck. Serum Ca 14·7 mgrm. At operation adenoma of parathyroid gland size of almond removed. No tetany, pains improved. Two months later serum Ca 12·1 mgrm., fresh cyst-like areas in radiograms of bones. Neck re-explored but no further tumour found. Patient treated with vigantol (irradiated ergosterol); great improvement, both clinical and radiological, although serum Ca 13·8 mgrm. and inorganic P 0·84 mgrm.

HUNTER (London, 1931).—Female, 37. *Case* 2 of present paper.

METHODS USED IN STUDY OF AUTHOR'S CASES.

Methods of the Metabolism Ward.—In our experience it has been impossible in the general hospital ward to attain accuracy of method which in any way approaches that of the laboratory. Our investigations have been carried out in a special metabolism ward under the care of an experienced Sister-Dietitian, and it is upon the painstaking and intelligent efforts of such a person that the accuracy of the work depends.

In the study of calcium metabolism it is necessary to know not only the level of calcium and phosphorus in the blood, but also the calcium and phosphorus balance; for just as the level of a river does not indicate the direction in which it flows, so the levels of the figures in the blood give us, in themselves, no indication whether calcium is flowing into excretory channels or into the tissues.

In our studies of endogenous calcium metabolism we assume a definite responsibility to the patient for the proper treatment of the disease under consideration, and we see that this has precedence over any investigations. The patient is given a diet containing only 100 mgrm. of calcium a day, but adequate in all other respects. This is necessary in order to reduce to a minimum the amount of unabsorbed calcium in the fæces. During the first few days the patient is allowed to choose whatever articles of diet seem most attractive from the limited list of foods low in calcium (Sherman, 1926; Simmonds, 1931). Emphasis is placed upon the fact that once a diet is chosen it cannot be changed during the period of study. Fluid and sodium chloride intake are kept constant, and distilled water is used in the preparation of all food and drinks. Sufficient sodium bicarbonate is given by mouth to make the reaction of the twenty-four-hour mixed urine neutral to phenol-sulphonephthalein (pH 7·3). The fæces are divided into three-day periods by the oral administration of 0·3 grm. of carmine alum lake every third day. Since constipation usually occurs on a low calcium diet we frequently employ liquid paraffin as a laxative. In some cases, where carmine does not appear in the stools within twenty-four hours, we use a simple enema made with distilled water. The urine is obtained in twenty-four-hour specimens.

Since inorganic salt excretion reaches a constant level only very slowly,

we endeavour to change our conditions of study not more than once in twelve days.

Preparatory to operation for removal of a parathyroid tumour the patient is kept on an unweighed high calcium diet. This includes four pints of milk daily, together with ice-cream, cheese, and eggs.

Laboratory Methods. — In estimating the blood-serum calcium the Kramer-Tisdall method as modified by Clark and Collip (1925) gives results with an average error of 2 per cent and a maximum error of 5 per cent. The normal figure by this method varies between 9·0 and 11·0 mgrm. per 100 c.c.

The distribution of phosphorus changes when blood is allowed to stand. Once the corpuscles have been laked, the liberated organic esters are very rapidly hydrolysed by the plasma phosphatase, and the concentration of inorganic phosphates rises rapidly. Samples of blood for estimation of the inorganic phosphorus must therefore be taken into oxalate, and any hæmolysed specimens must be rejected. With such precautions, using the method of Briggs (1924), the experimental error should not exceed 2 per cent.

In health the level of inorganic phosphate in the blood plasma varies between 2·5 and 3·5 mgrm. phosphorus per 100 c.c. In children, where ossification is more active, readings up to 5 mgrm. per 100 c.c. are found.

In 1929 Kay published a method for estimating the activity of the phosphatase in the plasma. He expresses this enzyme activity in terms of the number of milligrams of phosphorus liberated as inorganic phosphate from excess of sodium β-glycerophosphate in forty-eight hours at 38° C. and at pH 7·6 by 1 c.c. of plasma. Under these conditions the average value for normal plasma is 0·15 mgrm. In young infants the figure is higher.

The calcium estimations of both food and excreta were carried out by the method of McCrudden (1910).

Radiographic Methods.—In estimating the density of the radiographic shadows of bones it is found necessary to use a controlled method. A control subject is chosen of the same sex, age, weight, height, and build as the patient. The corresponding limbs of patient and control are placed side by side and exposed simultaneously on the same negative. Where a series of radiograms is taken in one patient the same control subject is used each time.

Histological Methods.—Wherever possible histological investigations of portions of bone and of parathyroid tumours have been carried out. The methods are indicated by Professor H. M. Turnbull in the reports on the corresponding cases.

CASE REPORTS.

Case 1.—**Hyperparathyroidism. Generalized osteitis fibrosa. Renal calculi.** (By the kindness of Dr. N. Hill and Dr. H. C. Lucey).

E. G., married woman, aged 49.

History.—Eight years, back began to bend. Shoulders became rounded. Gradual diminution of total height. Four years, multiple spontaneous fractures giving rise to deformities of limbs. Became bed-ridden. Admitted to Metropolitan Hospital, London, with spontaneous fracture of left humerus.

Past History.—Had pneumonia twice. Four children. Three alive and well. One died of tuberculosis.

On Examination.—Height, 4 ft. 9 in. Intelligence normal. Lies in bed

totally disabled, greatly deformed, breathless, and very wasted. Calvaria large. No tumour felt in neck. Angular curve in spine at level of 5th thoracic vertebra. Sternum and clavicles arched forwards. Collapse of ribs, causing the lateral diameter of the thorax to be greatly diminished and the antero-posterior diameter increased. Gross deformity of both upper limbs from mal-union of fractures. Signs of fracture of left humerus. Abdomen protuberant, subcostal margins approximated to iliac crests. Legs crossed scissor fashion owing to mal-union of fracture of left femur.

RADIOGRAMS.—Poverty of shadows of all bones examined, loss of detail and stippling. Atrophic changes, pale cyst-like spaces, and old fractures in bones of limbs. Kyphosis, collapse of ribs, and tri-radiate pelvis. Calvaria greatly thickened, blurred, and coarsely mottled. Large calculi in right kidney.

PROGRESS.—Progressive emaciation and exhaustion. Serum calcium 13·3 mgrm. per 100 c.c. Died following further spontaneous fractures.

POST-MORTEM (Dr. H. C. Lucey).—Bronchopneumonia. Gross changes in bones and parathyroid glands (*see below*). Three large irregular calculi in right kidney, with hydronephrosis and dilated ureter. No calculi in left kidney. Heart, liver, and spleen wasted. Larynx, trachea, œsophagus, suprarenals, pancreas, uterus, ovaries, and pituitary normal. No macroscopic evidence of metastatic calcification found in any organ.

COMPOSITION OF RENAL CALCULUS.—A portion of calculus taken for chemical analysis was friable and of a uniform white colour and consistency throughout its whole substance.

Chemical composition :—

Ca	24·4 per cent	CO_2	0·7 per cent
P	8·4 „ „	Oxalic acid ..	0·85 „ „

The calculus therefore consists principally of calcium phosphate, but there is more calcium than can be entirely accounted for by the acids. A comparison with the composition of bone is obviously of great interest.

Composition of bone :—

Ca	20·0 per cent	CO_2	3·25 per cent
P	9·0 „ „		

Pathological Report.

(PROFESSOR H. M. TURNBULL.)

Tissues sent by Dr. H. C. Lucey and Dr. N. Hill. (P.M. Appendix 496/1929.)

1. Bones.—

MACROSCOPIC.—

1. *Calvaria.*—This and the other specimens had been preserved by the Kaiserling process. The specimen was the posterior part of the roof of the skull removed by a coronal cut close to the fronto-parietal suture and a horizontal cut 1·5 cm. below the external occipital protuberance. The bone was greatly thickened and weighed 503·3 grm. It was 0·7 cm. thick at the junction of the two cuts, and rapidly thickened to 1·5 cm. upon the top of the skull and to 2 cm. in the mid-line below the occipital protuberance. The sawn surfaces were finely porous under a hand-lens, and red-purple. The grooves for the meningeal arteries were very deep ; the sutures were completely obliterated.

2. *Right Humerus* (*Fig.* 175).—The bone was greatly deformed, and measured only 25 cm. in a straight line from top to bottom. The shaft showed a conspicuous curve forwards after a sharp kink at the surgical neck and also a sinuous curve with the upper convexity outwards and the lower inwards. A fusiform expansion (3·3 cm. diam.) in the upper 9 cm. of the shaft was followed by a narrow portion (2 cm. diam.) for 3·5 cm., and this again by an expansion (3 cm. diam.) above the capitellum and trochlea. The lower expansion formed upon the anterior surface an oval, dark swelling (5 × 3·5 cm.) with an apparently membranous wall. The shaft was covered by an adherent layer of periosteum, tendon, and muscle. On the cut

surfaces revealed by sagittal section the tuberosities and the head showed a few small areas of soft yellow fatty marrow enclosed in a grey gelatinous tissue, which felt gritty and showed in places under a hand-lens a close, spongy bone. In the lower part of the tuberosities and in the surgical neck was an area of red marrow, free from bone. In the surgical neck this red marrow was bounded on each side by a layer (3 mm. deep) of grey gelatinous tissue that contained a delicate porous bone of slightly wider mesh than in the head. The red marrow extended as a wedge into the upper expansion of the shaft. The rest of the upper expansion contained five large and many small cysts of round or irregular shape. The cysts were often crossed by membranous trabeculæ, and were either empty or contained a deep-red jelly. The lining of the empty cysts was smooth and slaty grey. The larger cysts had a thick (2 mm. or more) wall of elastic grey tissue. Between the cysts was a little grey, gelatinous, tough, granular tissue mottled with red. Grey tissue containing spicules of bone, similar to that forming the

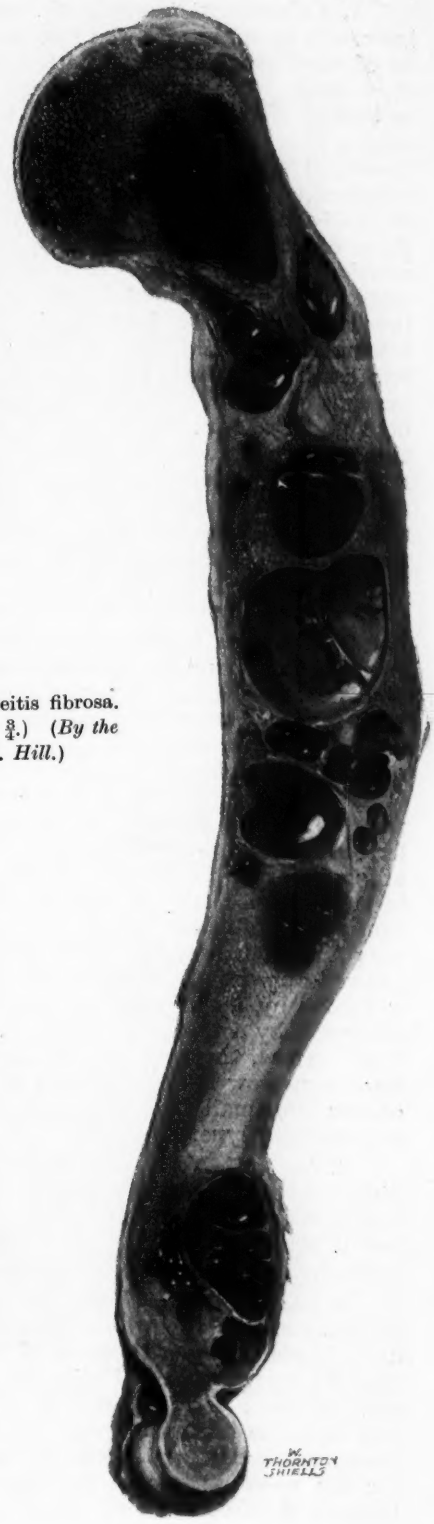

FIG. 175.—*Case* 1. Generalized osteitis fibrosa. Sagittal section of right humerus. (× ¾.) (*By the kindness of Dr. H. C. Lucey and Dr. N. Hill.*)

corticalis of the neck, lay beneath the periosteum over the cysts. It usually formed a mere shell, but at one spot on the anterior surface was a small patch 5 mm. thick and at another a longer segment 5 mm. thick. Beneath the latter patch was an area of yellow, fatty marrow. In the lower end of the upper expansion, beneath the cysts, the medulla was filled with soft red-brown tissue. In the narrow portion of the shaft the medulla contained yellow, fatty marrow. The corticalis here and outside the red-brown tissue above consisted, as in the neck, of grey gelatinous tissue containing a delicate spongy bone. Where fairly cut it was 4 mm. thick. In the lower expansion cysts similar to those in the upper were covered anteriorly by a gritty membrane and posteriorly by about 4 mm. of the grey gelatinous tissue containing spicules of bone. The wall between the fossæ above the trochlea consisted of a similar grey, gritty tissue; the trochlea contained a harder, finely porous bone and fatty marrow.

MICROSCOPIC.—Portions of the skull and humerus were decalcified in Müller's solution followed by nitric acid, and were stained by Schmorl's thionin methods, etc.

1. *Calvaria, at Summit of Coronal Cut.*—The bone is limited externally and internally by an interrupted line of slender trabeculæ. Between these lines trabeculæ of very irregular shape, either lying free or anastomosing, form a spongiosa of close mesh. The trabeculæ consist of a non-lamellar or woven bone. Part of this is typical coarse-fibred bone, in which the bundles of fibrils interlace at obtuse angles, the cell-spaces are closely packed, large and of irregular shape, and the canaliculi are scanty and short. Part is a bone in which the bundles of fibrils interlace at more acute angles and in places form an imperfect lamellation, whilst the cell-spaces and their canaliculi approach in number, arrangement, and shape those of perfect lamellar bone. Those two types of woven bone may be conveniently called *coarse-fibred bone* and *intermediate bone*. Where both occur in one system the coarse-fibred is central and merges into the intermediate, which may become imperfectly lamellar in its periphery. The imperfectly lamellar bone resembles that laid upon cartilaginous trabeculæ in infants; it is an immature lamellar bone. There is no perfect lamellar bone, such as is formed in the Haversian systems of adults. The larger trabeculæ usually show three or four systems in any field under a $\frac{1}{6}$-in. objective. A few trabeculæ contain small vascular canals, but there are no Haversian systems. There are numerous focal areas of resorption by many large osteoclasts. Active apposition is also focal. The osteoid zones are not abnormally deep. The marrow is fibrous throughout. The fibrosis is very uniform, and consists of numerous delicate collagenous fibrils and relatively few fibrocytes with narrow spindle nuclei. The vessels are engorged but are narrow. Near the outer surface is an oval cyst ($5 \times 2{\cdot}5$ mm.), which has a smooth margin bounded by a narrow zone of denser fibrosis.

2. *Head and Under Surface of Anatomical Neck of Humerus.*—There is a narrow layer of bone beneath the articular cartilage, and a very slender, interrupted, strip of bone beneath the periosteum of the neck. These layers of bone are bounded by a zone of fibrous marrow, except in a very few places, where they are in contact with adipose marrow. Within the head and neck is a remarkably small number of small, irregular, and slender trabeculæ. One or two of these are bounded by adipose marrow in part of their course. A few others are surrounded by a narrow zone of fibrous marrow. All the remainder are grouped within broad strands of fibrous marrow which form a net enclosing large areas of adipose marrow. The adipose marrow is in excess of the fibrous. In the few places in which the bone is in contact with adipose marrow it is almost invariably undergoing neither resorption nor apposition. Elsewhere active resorption is very great. Osteoclasts are very numerous both upon and close to the surfaces of trabeculæ, which have a very gnawed appearance owing to the number of Howship's lacunæ. Active apposition is shown by numerous large osteoblasts upon osteoid zones. It is greatly overshadowed by active resorption. Where the osteoid zones are cut at right angles to their surface, they are not deeper than in the long bones of healthy infants. The fibrous marrow is slightly more cellular than in the skull. With the exception of one or two small fragments of lamellar bone the bone is woven and mostly of the intermediate type.

3. *Surgical Neck.*—The corticalis is replaced by a sharply defined layer of fibrous marrow within which lie scattered a few small trabeculæ of woven bone. Active resorption by osteoclasts is again very great. Active apposition is present but is relatively slight. The medulla consists of adipose tissue which is injected throughout and contains numerous foci of hæmatogenous activity.

4. *Shaft between Upper and Lower Expansions* (*Fig.* 176).—The longitudinal section includes the whole thickness of the bone. The corticalis on each side is again replaced by a layer of fibrous marrow, which is of even depth and has a straight inner margin. Under the periosteum on each side is an interrupted, narrow strip of bone. This is lamellar on the outer side but woven on the inner. Beneath this strip the fibrous marrow contains trabeculæ which are in general slightly more numerous and larger than in the surgical neck. They consist of woven bone, which for the most part is of the intermediate type and frequently becomes lamellar towards the free surfaces. One or two Haversian systems are being formed within

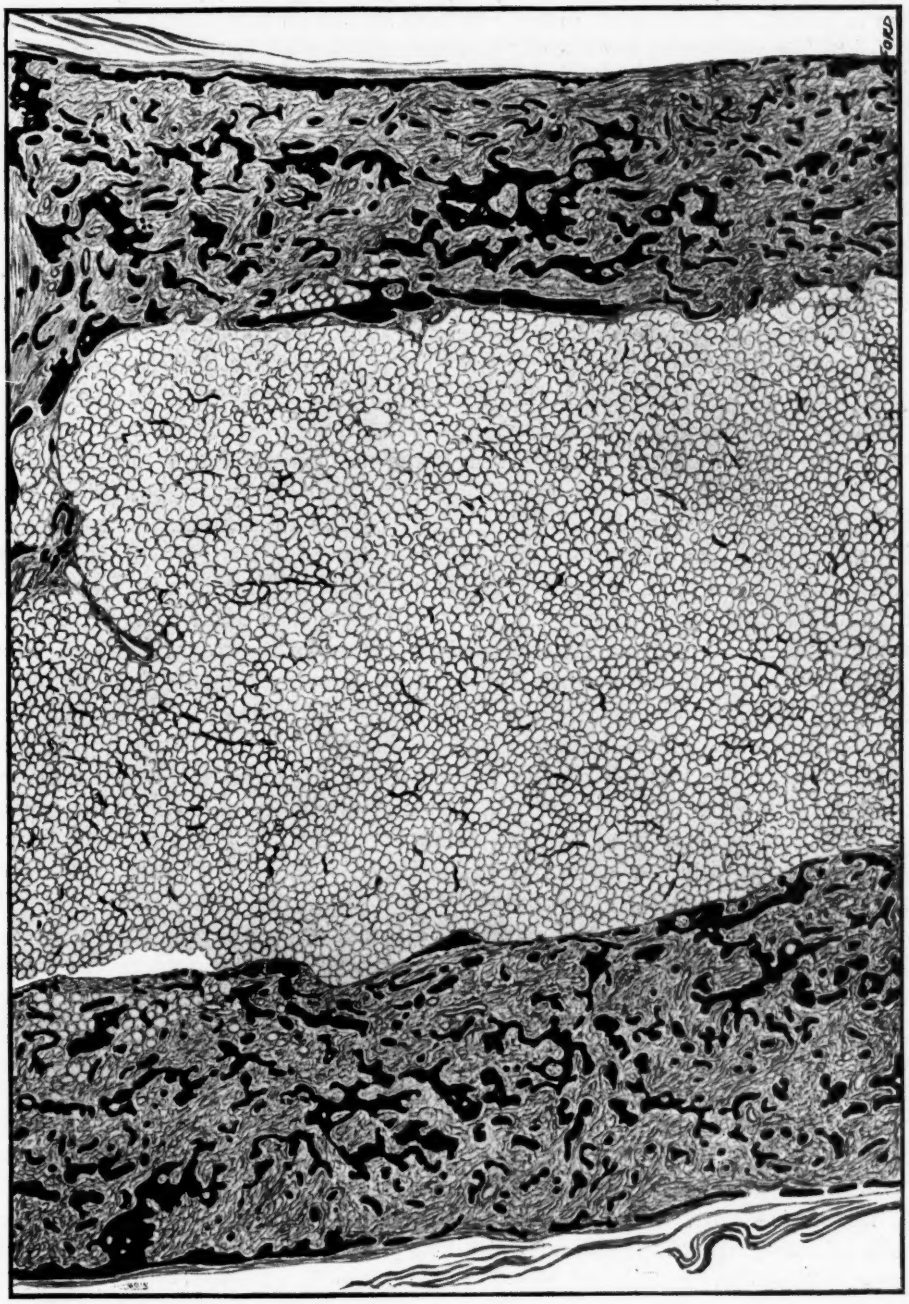

FIG. 176.—*Case* 1. Longitudinal section of entire shaft near centre of humerus, to show the strict limitation of the fibrosis to the altered corticalis. Generalized osteitis fibrosa. Müller's fluid followed by nitric acid; Weigert's iron-hæmatoxylin and van Gieson.

the largest trabeculæ. The trabeculæ are composed of fewer separate systems than in the skull. In many places there are numerous osteoclasts in Howship's lacunæ and in the adjacent marrow. There are also many osteoid zones covered by a layer of closely packed, large osteoblasts. The osteoid zones are of about the same depth as in infants. The fibrous marrow is very similar to that in the head of the humerus, but the capillaries are slightly widened, there are a few hæmorrhages, and there are many groups of cells loaded with iron-pigment. Further, there are small focal areas in which the marrow is not fibrotic and contains hæmatogenous marrow. The medulla contains adipose tissue.

Remarks.—The most conspicuous feature in the bones examined is resorption. Resorption was very active at the time of death, especially in the cortex of the humerus. Past resorption is obvious in view of the replacement of the compacta of the skull and humerus by small isolated trabeculæ. In the humerus extremely little bone remains. All perfect, adult lamellar bone has been removed from the skull and humerus, except possibly some small fragments beneath the periosteum of the humerus. The bone that is now present is almost all woven bone which is partly typical coarse-fibred bone and partly a woven bone that has been described above and called 'intermediate bone'. The coarse-fibred bone merges into the intermediate bone, and the latter merges into a lamellar bone which is most perfect in the corticalis of the narrow portion of the shaft of the humerus. Coarse-fibred and intermediate bone are found in the fundamental systems of the long bones of adults. Since, therefore, resorption usually commences in Haversian systems and extends to fundamental systems, portions of such bone are likely to remain longest. The amount and distribution of the woven bone in this case, however, make it impossible for it all to be remnants of fundamental systems. Further, much is obviously of recent formation. There can be little doubt that most of the bone present, probably all in the skull, represents bone which has been formed during the disease. It follows that resorption has cleared away almost all, if not all, the normal bone, and that this great resorption has been associated with apposition. That the two processes have continued side by side for a considerable time is shown by the mosaic of systems in the trabeculæ. The number of systems is small in the small trabeculæ of the humerus, but is moderately great in the larger trabeculæ of the skull. At the time of death active apposition was taking place throughout the bones examined, but is overshadowed by the active resorption. The number and size of the osteoblasts upon the osteoid zones point to a rapid apposition. The depth of the osteoid zones is not greater than in healthy infants, so that in view of the rapidity of apposition there is no evidence of osteomalacia. When sections such as these are examined it is not difficult to understand how bones formed by trabeculæ isolated in a fibrous matrix can bend without any softening of the trabeculæ.

A fibrous marrow is present throughout the calvaria, throughout the corticalis of the shaft of the humerus, and in part of the spongiosa of its head and neck. The distribution of the fibrous tissue is closely connected with the osseous portions of the bones. In the shaft of the humerus it replaces the original corticalis and is sharply limited from the adipose or hæmatogenous marrow of the medulla (*Fig.* 176). In the head and neck of the humerus it forms strands enclosing groups of bony trabeculæ or forms a zone round

single trabeculæ. A few trabeculæ are in part of their course in direct contact with adipose marrow on one or both sides. At such spots active resorption and apposition are very rare, but do occur. These appearances, which I have seen in other cases, suggest that the fibrosis of the marrow is merely an expression of exceptional activity in the osteogenetic marrow.

The cysts in the humerus were not examined microscopically, but a small cyst was accidentally found in the skull. Its structure gives no indication of its mode of formation.—H. M. T.

2. Parathyroid Bodies.—

MACROSCOPIC.—The specimen was a thyroid gland (*Fig.* 177) from which had been sliced off the posterior parts of the left lateral lobe. The cut surface of the thyroid gland was dark and glistening. In a concavity in the upper pole of the left lobe was the cross-section of a sharply defined yellowish-white sphere 1·1 cm. in diameter. This was covered externally by a transparent capsule, which swept in as a narrow grey line between it and the thyroid tissue. Projecting into the lower pole of the right lobe from the posterior border was a yellowish-white mass, 2·8 cm. high, 1·8 cm. from before back, and about 2·5 cm. from side to side. The outer surface was nodular and covered by a transparent capsule. The cut surface showed a central, granular, gritty, yellow area, from which one or two calcareous spicules projected. Round this was a zone of smooth, pale yellow tissue separated into rounded lobules of about 3 mm. in diameter.

FIG. 177.—*Case* 1. Generalized osteitis fibrosa. Thyroid gland showing in section smaller tumour of left superior parathyroid body and larger tumour of right inferior parathyroid body. (*Actual size.*) (*By the kindness of Dr. H. C. Lucey and Dr. N. Hill.*)

MICROSCOPIC.—The *left upper parathyroid body* is surrounded by a capsule of dense collagenous fibrous tissue and elastic fibres, which shows a few calcareous plaques in its inner aspect. Within this it is divided into small acini by a net of capillaries, walled by a sheet of collagen. In three small areas the collagen is greatly swollen and hyaline, whilst the capillary lumina are obliterated, so that stout hyaline nets are formed enclosing small remnants of acini. Throughout much the greater part of the gland the acini contain polygonal cells with a deeply oxyphil, eosinophil, cytoplasm. This cytoplasm is almost always vacuolated, but the vacuoles are usually very small, so that the cells typically have a solid, granular appearance, recalling hepatic cells. The cells measure in mean diameter 7 to 11·5 μ. Their nuclei are round or slightly oval. They usually measure 4 to 5 μ, but variation in the size of the nuclei is conspicuous; many measure up to 7 μ, and there are a very few of 9·5 μ. Most are very deeply stained. They show a stout membrane, a widely meshed net of chromatin, large rounded nodes, and occasionally, one or more nucleoli. In sharp contrast to the main part of the gland are a few scattered groups of acini which contain smaller, greatly vacuolated cells. These cells measure from 6 to 9 μ. Their nuclei are usually 4 μ, rarely as large as 6 μ; the larger examples are less deeply stained. They show a basophil reticular cytoplasm and a basophil cell-membrane (pyronin-methylgreen). Occasionally a faintly stained oxyphil substance can be seen in the meshes of the reticulum. Most of the cells are very dropsical, showing little or no cytoplasm except the cell-membrane. Some of these acini contain a few of the deeply oxyphil cells also.

In the adjacent thyroid gland most of the acini are large and filled with colloid,

whilst the epithelial cells are sharply defined and flattened. In other acini there is little or no colloid, and the cells are ill-defined.

The *right lower parathyroid body* is divided into large rounded and oval lobules by stout septa, which consist of collagen and elastic fibres and are frequently bounded internally by a sheet of elastic fibres. The peripheral lobules project into the surrounding areolar tissue, being frequently separated to a considerable extent by wedges of areolar tissue containing large vessels, and their free convexities are encapsulated by continuations of the septa. One large and several small lobules lie apparently free in the areolar tissue at a considerable distance from the main mass. Other small lobules appear to be isolated within septa. The capsules of the isolated lobules are nowhere lined with endothelium. The septa contain veins and a few arteries. The lobules are more or less completely subdivided into acini by the walls of numerous branching veins and capillaries (Laidlaw's and van Gieson's stains). The acini are usually of large size and are frequently long and narrow. In one lobule there are large areas in which the collagen of the veins and capillaries is greatly swollen and hyaline, and forms hyaline nets like those seen in the left body. Most of this hyaline tissue is calcified. In the centres of the areas the remnants of acini within the calcified net are frequently necrosed and often are calcified. The septum bounding this lobule, and some adjacent septa, are also hyaline and extensively calcified. In this body deeply oxyphil cells are very scanty. Usually they are scattered singly throughout the gland, but sometimes they form small groups. They are of similar size to those in the left. Basophil cells greatly predominate. They measure from 4·5 to 12 μ. Most are between 9 and 12 μ and are dropsical, the cytoplasm being reduced largely or entirely to a cell-membrane. The nuclei are usually 4 μ in mean diameter, but there are a few giant oval nuclei up to 10·5 μ. Most of the nuclei are pale. In places these dropsical basophil cells are of long, narrow columnar shape, e.g., 20 × 3 μ. They are then arranged sometimes in a palisade between two vascular septa, sometimes as the sharply defined wall of a cleft that contains a few free rounded cells. Cubical basophil cells occasionally surround a small sphere of oxyphil coagulum.

In a small piece of thyroid gland the colloid is less deeply stained than on the left, and the cells are not flattened.

Remarks.—In order to compare the cytology of this and the subsequent enlargements with that of normal parathyroid bodies some account of the latter is necessary. The measurements given are mean diameters in paraffin sections of a series of glands fixed in formaldehyde.

The normal parathyroid glands.

Welsh (1898) divided the cells of the normal gland into oxyphil* cells and principal cells; he subdivided the latter into four types according to their form and arrangement. Erdheim (1903) described two kinds of oxyphil cells: the large pale and the small dark. According to Erdheim (1901) oxyphil cells occur first in the tenth year, and are present in variable number ever after. My own series agrees with this, but only one year, the fifth, is represented between the second and the thirteenth. There is no difficulty in distinguishing these three types of cell: the dark oxyphil, the pale oxyphil, and the principal.

The *dark oxyphil cells* are in general the rarest. They are frequently absent when the pale type is present, and it is exceptional to find them forming large groups. They are usually found in small number, both among the principal cells and in contact with pale oxyphil cells. The latter is their

* Welsh actually wrote "oxyphile."

favourite position. When present in groups of pale oxyphil cells they recall crescents in mucous glands. They measure from 7 to 12 μ in mean diameter, usually being about 9·5 μ. The cytoplasm looks dense and granular. Under high magnifications it shows scattered vesicles of different sizes; I have not detected true granules in fixation with formaldehyde, Zenker, or alcohol. It is stained deep red or purplish red by hæmatoxylin and eosin, and dark green by pyronin-methylgreen. No net formed by cell-membranes is seen between adjacent cells, but in sections stained with pyronin-methylgreen a pink membrane sometimes bounds the cytoplasm of an occasional cell. The nucleus measures 3·5 to 5 μ. Except when of the largest size, it is usually deeply stained but shows a clear structure.

The *pale oxyphil cells* (*Fig.* 190) usually form a variable number of nodules that are conspicuous under low powers; with higher magnifications others are found singly or in small groups. The cells measure from 9·5 to 17·5 μ, but are usually from 12 to 15 μ. The cytoplasm is very characteristic, consisting of evenly distributed small spherical granules. The membranes of adjacent cells form a sharply defined net of perfectly polygonal mesh. The cytoplasm is stained a bright warm red or a paler pink by hæmatoxylin and eosin; in pyronin-methylgreen it is stained pale blue-green, but the membranes are stained pink. More deeply stained red particles sometimes lie on the pink membrane and project into the cytoplasm; rarely a similar particle lies isolated within the cytoplasm. I have not yet detected glycogen in the cytoplasm of these cells in normal material from the post-mortem room, but I have found it in similar cells in enlarged glands removed by operation. The nuclei measure from 3·5 to 7 μ, but 7 μ is very exceptional and 4 to 5 μ is usual. The smallest nuclei are found in the larger cells and are pyknotic. The pale oxyphil cells sometimes surround small alveolar spaces filled with acidophil coagulum.

The *principal cells* differ according to their degree of vesiculation. They vary in size from 6 to 15·5 μ. The smaller cells are least vesiculated. Their cytoplasm consists of an irregular net of particles of cytoplasm of different sizes. As vesiculation increases a cell-membrane becomes visible and the cytoplasmic net becomes ever more scanty until completely dropsical or ballooned cells are formed in which the nucleus lies free in a cavity bounded by a membrane (*Fig.* 183). The meshes of the net of membranes between adjacent ballooned cells are less perfectly polygonal, being more rounded, than those between pale oxyphil cells. The cytoplasm is stained a blue purple by hæmatoxylin and eosin. In pyronin-methylgreen the membrane and cytoplasmic net are pink, some large particles in the net usually being a deeper red. A very pale blue-green ground can be recognized in some cells. The principal cells are, therefore, essentially basophil. Glycogen is found in them, and is most abundant in the dropsical examples. The nuclei measure from 4 to 5·5 μ. They are usually lightly stained, but tend to be dark in the smaller cells. Alveolar spaces filled with acidophil coagulum are bounded more frequently by principal cells alone, or by principal cells and one or two dark or pale oxyphil cells, than by pale oxyphil cells alone. Those bounded by oxyphil cells alone are usually smaller.

Nature of above Types of Cell.—Although the dark and pale oxyphil cells

and the principal cells are easily differentiated, particularly in sections stained with pyronin-methylgreen, the three types appear to represent conditions of special activity, or conditions of exaggeration of a particular activity common to all, rather than to be cells of distinct origin and nature. Evidence of the origin of oxyphil cells from principal cells is found in the absence of oxyphil cells in the fœtus and young child, the variation of their number in older subjects, and the sporadic presence among principal cells of single dark or pale oxyphil cells of similar shape and only slightly larger size. Further, pale oxyphil cells can apparently lose their peculiarities and become indistinguishable from ballooned glycogen-containing chief cells. Thus, not only are pale oxyphil cells often found within groups of ballooned cells, but sometimes in a nodule of pale oxyphil cells morphological transitions are found to completely dropsical cells with a basophil membrane from cells with a typical finely and evenly granular pale oxyphil cytoplasm and basophil membrane through cells with a similar cytoplasm broken to different degrees by large clear vesicles. There can be little doubt that dark and pale oxyphil cells are closely related. When cells of both types are present most of them lie in direct contact. Further, the depth of staining by eosin varies in different groups of pale oxyphil cells, the more deeply stained being of smaller size and having their cytoplasmic granules more closely packed. That oxyphil cells merely represent an exaggeration of an activity possessed by principal cells is suggested by the pale variety, and occasional examples of the dark, showing a basophil membrane, whilst a pale oxyphil substance can be detected in the basophil net of some principal cells. Further, the basophil cytoplasmic net of the principal cells usually contains more deeply basophil particles, whilst similar particles sometimes lie upon the basophil membrane of pale oxyphil cells and occasionally lie isolated within the oxyphil cytoplasm. The appearances suggest that the oxyphil cells are principal cells in which the cytoplasm has been so charged with oxyphil granules that the basophil net has been more or less completely reduced to a limiting membrane.

The parathyroid glands in present case.

In the present case the structure of the right parathyroid gland suggests an enlargement by an addition of lobules in the periphery rather than by a simple expansion. There is no evidence, however, that the enlargement has been associated with destruction of tissue or permeation of channels lined with endothelium. The structure can be explained by successive enlargement of the lobes of a segmented gland, a process which is taking place in the smaller parathyroid gland of *Case* 4. In both glands retrogression is indicated by hyaline degeneration of vessels. This is very slight in the left gland, but is considerable in the centre of the very large right gland, and is here complicated by calcification. Such retrogression is not proof of true neoplastic growth; severe degenerations occur in colloidal goitre, which is not definitely a neoplasm. The cells are of kinds found in normal glands: the only abnormalities are the cylindrical principal cells of unusual height and the giant nuclei. Cylindrical principal cells are found, however, in normal glands, and the mean diameter of these exceptionally elongated examples falls within normal limits. Giant nuclei are found in hyperplasias

that indicate abnormal functional activity; they are conspicuous in many thyroid glands in Graves' disease. There is, therefore, in the gross and minute structure of the two enlarged parathyroid glands nothing that indicates autonomous neoplasm rather than functional hyperactivity. In the hyperplasia there has been a very great increase of dark oxyphil cells; in the right gland their mass greatly exceeds that of all four glands in a normal subject. Principal cells in the dropsical or ballooned state form, however, a far greater proportion of the total mass of the two glands. Unfortunately no material was available for the detection of glycogen, which is usually abundant in ballooned principal cells.—H. M. T.

Case 2.—**Hyperparathyroidism. Generalized osteitis fibrosa with multiple osteoclastomata. (Hunter, 1931).**

M. F. R., single woman, aged 37. (L.H. Reg. No. 40737/1930.)

HISTORY.—Born in Greenwich. Employed in post office from 1908 (when aged 15) till March, 1928.

Summer, 1925.—While on holiday (chiefly walking) along Rhine valley, had slight injury to right foot making the arch painful for a few weeks. Continued to walk and was otherwise well.

May, 1926.—Slight pain in knees, hips, heels, and in arms. Weakness and lack of energy. Unable to walk any distance; had to give up tennis but was able to work. Occasionally cried with pain on shaking hands.

May, 1927.—Seven weeks' holiday on account of pain in legs and knees.

September.—Pain much worse in hips, knees, and heels. Legs and thighs unaffected. Pain never prevented her from sleeping, was worse when she moved about. In bed for seven weeks. Temperature was normal, but she was thought to be suffering from rheumatism. Pain and weakness occurred in the arms, and she had to give up work because she was unable to stoop or lift the heavy ledgers.

February, 1928.—Hardly able to get about because of pain and weakness. Unable to get up from a chair or to walk with aid of a stick. Slight swelling of jaw was noticed. Right hip was now the site of worst pain. Improved slightly, went back to work half-time for two months.

March.—Had to leave work permanently.

June.—Slipped from her chair and was doubled up at the hips. Had to be lifted up and has not walked since. Great stiffness of lower limbs, hips becoming very painful and knees remaining straight. Admitted to Greenwich and Deptford Hospital, where she remained in bed for five weeks. While under treatment she noticed a swelling of the left forearm and another on the back of the right hand. Mercury ointment was rubbed into these without effect. Radiograms taken of jaw and of both hip-joints. She was told that there was no fracture, but that the bones were very thin. Had massage at home for three months.

Oct. 28.—Admitted to Guy's Hospital. Weight, 5 st. 5 lb. 8 oz.

Nov. 14.—Accidentally thrown from a wheel-chair. Painful injury of right forearm.

Radiograms of Bones.—"All bones very translucent. Fracture of right radius and ulna. Shaft of left ulna shows cavitation and expansion of cortex. Ribs collapsed. Destruction of bone in third right metacarpal, both sides of mandible, necks of both femora and left iliac bone."

Urine.—Neutral; sp. gr., 1010; trace of albumin; Bence Jones protein absent; no sugar; deposit of phosphates.

Blood-count.—Red cells, 4,460,000; white cells, 15,000; polymorphonuclears, 70 per cent.

Feb. 1, 1929.—Portion of tumour of mandible removed for histological section. Easily cut with a knife. Dr. G. W. Nicholson reported upon the histology: "A giant-celled epulis".

Feb. 4.—Serum calcium 15 mgrm. per 100 c.c.; plasma phosphorus 3·3 mgrm. per 100 c.c.

Treatment: Right forearm immobilized in plaster for six weeks. Fractures united. Cod-liver oil given over a period of ten weeks in increasing doses, up to six drachms three times a day. During the last seven weeks of this treatment irradiated ergosterol was given; continued for three months, dose increased to 10 min. three times a day (radiostoleum). When the cod-liver oil was discontinued ultra-violet irradiation was used three times a week. Deep X-ray therapy applied to the bones (seven exposures).

March 5.—Left hospital.

April.—Noticed swelling on inner side of right leg below knee.

May 25.—Re-admitted to Guy's Hospital. Weight 4 st. 5 lb. 10 oz. Tumours of jaw and right hand larger.

Radiograms of Bones.—"Heads and necks of both femora appear to be absorbed and trochanters displaced upwards. Pelvis shows collapse and absorption of bone salts, more marked on right side."

Treatment: Four applications of deep X-ray therapy to jaw and arms. Insertion of radium into mouth.

July 5.—Left hospital.

October.—Had to give up writing and sewing.

April, 1930.—Re-admitted to Greenwich and Deptford Hospital. Further radiograms taken. Density of bone-shadows extremely poor. Many tumours expanding bone. Dr. Macdonald Critchley saw the patient in consultation with Dr. W. Denison Wiggins and diagnosed hyperparathyroidism.

Past History.—No history of rickets as a child. Catamenia began at age of 14; usually lasted a week. Normal until June, 1927, then somewhat excessive until June, 1928, when they suddenly ceased for eighteen months. Then irregular for six months and ceased entirely after April, 1930. In 1916 many teeth extracted for caries, leaving only eleven; in 1926, eight more teeth extracted. No history of polydipsia, polyuria, renal pain, or passage of stone or gravel. In 1923, while playing tennis, fell on outstretched hand and fractured left radius. Arm was in splint for ten days and bone united within a month.

Family History.—Father, one brother, and one sister, alive and well. Mother died from carcinoma of colon. No family history of fractures, dislocations, blue sclerotics, deafness, or peculiar shape of head.

May 28, 1930.—Admitted to the London Hospital.

On Examination.—Height, 4 ft. 10 in. Weight, 4 st. 13 lb. Patient is intelligent and gives a concise history. Lies in bed totally disabled, deformed, frail, and wasted. Hips and knees flexed. Able to move left leg, but cannot straighten right leg. Unable to move either arm. Left arm aches. Great pain in right hip if she is lifted on that side. Pressure upon the bones, especially the forearms, gives rise to pain and this is severe when she is turned in bed. Sclerotics white. Lenses normal on examination by slit lamp. Hearing normal. Tongue clean. Mucous membranes normal colour. Thyroid gland normal. No tumour felt in neck. Forehead prominent, but skull otherwise normal. Hard, non-tender, bony enlargement on right side of mandible forming a swelling, 6 cm. in diameter. In the skin over it is a surgical scar. Tumour protrudes into mouth, where it is covered by bluish-red buccal mucosa. Only three teeth remain and appear to be normally calcified. Thorax tapers in upper part, superior inlet being thus reduced in diameter. Normal prominence of shoulders is missing, so that arms seem to disappear into upper part of chest, and clavicles to be too prominent. Lower thorax widens out, subcostal angle being normal. Eight slightly tender bony nodules felt in course of ribs, especially lower ribs. Slight scoliosis. Arms extremely thin, owing to muscular wasting and to diminution in total width of bones, are crossed upon chest; range of voluntary movement limited to a few inches. Antero-external curvature of both forearms. Upper end of left ulna presents a bony swelling. Large, slightly tender, bony swelling 4 cm. in diameter on dorsum of right hand apparently arising in third metacarpal. Second left metacarpal distorted and thickened. On passive

movement shoulder-joints are free, except in extreme abduction, which causes pain. Free flexion of elbow-joints is possible, but not full extension. Voluntary movements of left hip and knee are good. Marked abduction of left hip and complete extension of both knees give rise to pain. Movements of right hip limited. Sharp antero-posterior curvature of the upper end of right tibia and fibula with its concavity forward. Left lower limb not deformed. Bones of lower limbs not shortened.

FIG. 178.—*Case* 2. Controlled radiogram of right forearm.
(Reproduced by permission of the Royal Society of Medicine.)

Heart, lungs, and abdomen normal. Blood-pressure 140/100 mm. mercury. Generalized wasting and slight hypotonicity of muscles. No abnormality in nervous system. Trousseau and Chvostek signs absent. Wassermann reaction negative.

Urine.—Alkaline; sp. gr., 1014; albumin, heavy cloud; Bence Jones protein absent; no sugar. Deposit of amorphous and triple phosphates. Average daily output of urine (May–June, 1930) was 765 c.c.

Renal Efficiency Tests.—Blood urea 0·033 per cent.

	c.c.	PHENOLSULPHONEPHTHALEIN Percentage	UREA CONCENTRATION Percentage
First hour ..	46	28·6	1·26
Second hour ..	85	16·6	0·96

Blood-count (May 20, 1930).—Red cells, 4,400,000; Hb, 50 per cent; C.I., 0·55; leucocytes, 4920; differential count, normal; bleeding time and coagulation time, normal.

Radiograms of Bones (*Fig.* 178).—Greatly diminished density of shadows of all bones examined. This is emphasized by contrast with the bones of a control subject. Scoliosis. Collapse of chest wall with thinning of ribs and clavicles. Extremely diminished density of shadows throughout lumbar spine and pelvis. Both hips abnormal in position. The heads and necks of both femora have disappeared. Calvaria is mottled and shows two rounded pale areas with ill-defined

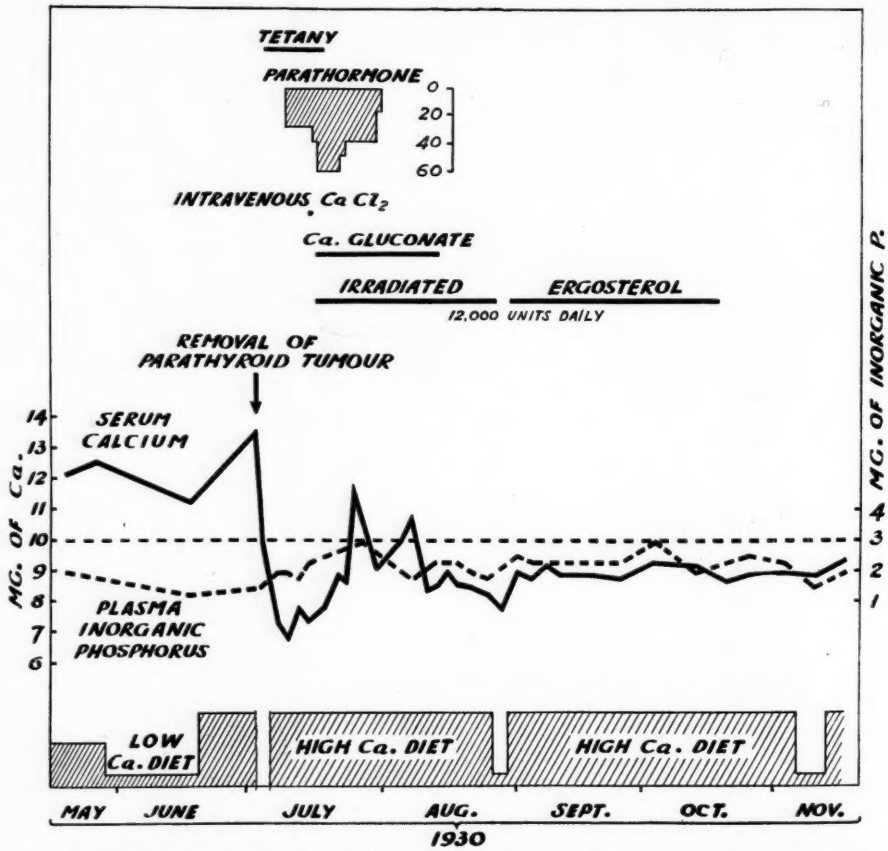

FIG. 179.—*Case* 2. Chemistry of the blood. The blood was examined at intervals for two months before and for five months after operation. The low calcium diet was that given during the investigation of the calcium balance. The high calcium diet was not weighed. It included four pints of milk daily, together with ice cream, cheese, and eggs. The scale indicating the dosage of parathormone represents units per day. The dosage of intravenous calcium chloride was 10 c.c. of a 5 per cent solution. The dosage of calcium gluconate was 10 c.c. of a 10 per cent solution daily, given by intramuscular injection. The dosage of irradiated ergosterol was measured in antirachitic rat units.

borders. Tumour of mandible dense and coarsely trabeculated. Head of right humerus has almost disappeared. Left humerus, right tibia, and right and left radius and ulna are bowed, frail and narrow, and show a grossly deficient corticalis. Irregular, pale, trabeculated areas expanding the corticalis are seen in right and left ulna, in several phalanges, and in second left and third right metacarpals. The last-named is so large as to distort the adjacent second and fourth metacarpals. Fracture of second metacarpal through a pale, cyst-like area at its mid-point.

Radiograms of Kidneys.—Kidney shadows normal in size. Two groups of small calculi seen in region of right kidney.

Calcium and Phosphorus Metabolism before Operation.—Hypercalcæmia was constantly present, the serum calcium varying between 11·2 and 13·6 mgrm. per 100 c.c. (*Fig.* 179). The corresponding figure for plasma phosphorus was 1·3 mgrm. per 100 c.c. Plasma phosphatase 1·13 mgrm. The calcium output was estimated in the urine and fæces for three three-day periods. The patient was kept on a weighed diet of known low calcium content. The calcium output in the urine was about three times the normal, that in the fæces being approximately normal (*Fig.* 180).

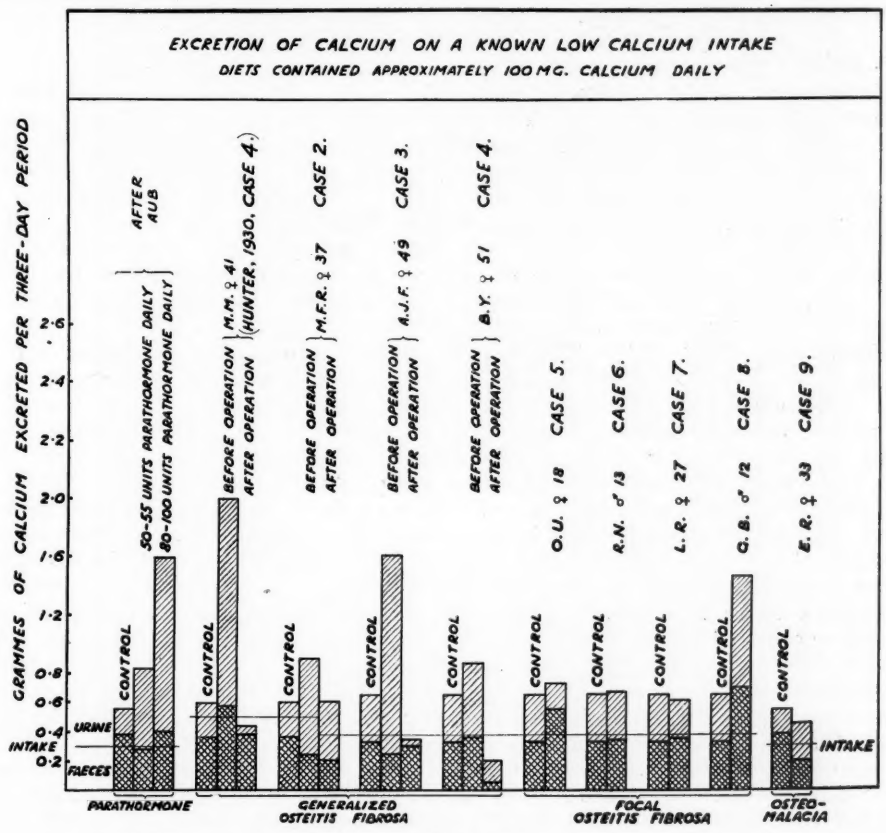

FIG. 180.—Calcium balance in generalized osteitis fibrosa, focal osteitis fibrosa, and osteomalacia. (The effects of injections of parathormone in normal individuals are shown in the first three columns.) The calcium excretion was estimated on a known low calcium intake. The horizontal lines represent the calcium intake, which was approximately 100 mgrm. daily. The urinary calcium excretion is represented by single cross-hatching and the fæcal calcium excretion by double cross-hatching.

OPERATION (Mr. A. J. Walton—July 2, 1930).—Under open ether anæsthesia collar incision made in neck. Sternomastoid muscles were retracted on either side and pretracheal muscles divided. Thyroid gland apparently normal; inferior pole of left lobe was explored, and a normal left inferior parathyroid gland identified. The left superior parathyroid body, embedded in the posterior aspect of the upper pole of the left lobe of the thyroid gland, was dissected out with a blunt dissector. It was enlarged and measured approximately 1·4 × 0·8 × 0·5 cm. Its blood-supply was left intact. Exploration of the inferior pole of the right lobe of the thyroid gland failed to reveal the right inferior parathyroid body. An irregular projection from the lateral surface of the right lobe of the thyroid gland in its

upper part was dissected out and removed. As this was completed a tumour was unexpectedly displayed projecting from behind the trachea in the situation of the right superior parathyroid body. This was a smooth, solid, oval, brown-yellow tumour measuring 2·3 × 1·5 × 0·9 cm. It was removed. One drainage tube was inserted and the wound closed.

A portion of bone was removed from the upper part of the shaft of the right tibia.

Pathological Report.

(Professor H. M. Turnbull.)

Tissues removed at operation. (S.D. 1518/1930.)

1. Right Tibia.—

Macroscopic.—The specimen was a longitudinal slice from the upper part of the shaft. It was 3·5 cm. long. The outer border was covered with periosteum. In the lower 2 cm. the cut surface was 0·6 cm. wide and consisted of a gritty grey tissue, in which minute spicules of bone were seen with a hand-lens. It gave the impression of a closely-meshed spongiosa formed by very delicate trabeculæ. In the upper 1·5 cm. the periosteal border bulged and was easily indented with a finger-nail. The cut surface was 1·1 cm. wide, and consisted of a rubbery grey gelatinous tissue in which no bone was seen. The slice consisted, therefore, of a lower, bony, and an upper, fleshy, segment. It was divided for microscopic examination through the bony part with great ease with a scalpel.

Microscopic (*Fig.* 181).—The two pieces were completely decalcified almost throughout with Müller's solution. In the lower, bony, segment there is no corticalis. The bone throughout consists of discrete branching trabeculæ of bone in a relatively abundant fibrous marrow. The fibrous marrow is very uniform, and consists of closely-packed collagen fibrils, numerous spindle fibroblasts with oval nuclei, and vessels of normal structure. In places the vessels are dilated. Towards the medullary cavity the fibrous marrow encloses a very few small islands of adipose tissue. Any bony trabeculæ that impinge upon this adipose tissue are surrounded by a zone of fibrous marrow. The trabeculæ are slender throughout the bone, but they are specially slender in the subperiosteal third. In a few trabeculæ towards the medulla there is a small portion of perfect lamellar bone. Otherwise the trabeculæ consist of coarse-fibred and intermediate bone, and seldom contain more than one system. Active apposition is shown by numerous osteoid zones, on which the osteoblasts are large and close together. Where the osteoid zones are shown by the shape of the osteoblasts to have been cut strictly at right angles to their surface, they are not deeper than those seen in healing fractures. There are very few osteoclasts in Howship's lacunæ until the upper, fleshy, part of the specimen is approached. Then many are seen in places, particularly in a narrow area immediately beneath the periosteum. In this area spindle fibroblasts are much more numerous in the marrow, groups of lymphocytes infiltrate the marrow, bony trabeculæ are very few and small, and numerous osteoclasts lie upon or near them. Bone is being laid down, however, upon these trabeculæ wherever osteoclasts are absent.

The upper, fleshy, segment is divided by strands of fibrotic marrow into lobular areas of cellular marrow crowded with giant cells. In the cellular areas spindle fibroblasts predominate, but there are many rounded, polygonal, and stellate forms. One karyokinetic figure was seen. Collagen and reticulum fibrils are usually scanty. There is a sparse infiltration with lymphocytes, monocytes, and occasional neutrophil leucocytes. Here and there are small groups of cells laden with iron pigment, and a diffuse impregnation with iron of the periphery of some lobules is shown by the Prussian-blue method. The vessels are capillaries bounded by a single or double row of cells. There are a few groups of extravasated red corpuscles, and more numerous very small areas of the fibrinous imbibition that, in association with extravasations, is so conspicuous a feature in most 'red tumours'. The giant cells resemble osteoclasts. They are very numerous, and most are very large. A few

are so deeply stained throughout that few of their nuclei can be recognized. Some have one or more large vacuoles in their cytoplasm, several contain an ingested monocyte or neutrophil leucocyte, a few contain a rounded group of red corpuscles. The cellular marrow in the lobules merges into the fibrotic strands which separate the lobules from one another and from the periosteum. In these strands the marrow usually resembles that which predominates in the bony segment, but is more cellular

FIG. 181.—*Case* 2. Right tibia. Junction of lower, bony, segment with upper, fleshy, segment containing osteoclastomata; periosteum on top. Generalized osteitis fibrosa. Müller's fluid; Weigert's iron hæmatoxylin and van Gieson.

in the greater part of the strand beneath the periosteum. It usually contains trabeculæ of woven bone bounded by osteoid tissue. Trabeculæ of osteoid tissue alone are also seen, but comparison of serial sections shows these to be tangentially-cut osteoid zones upon calcified cores. The trabeculæ resemble the more slender of those in the bony segment. The osteoid zones appear to be of similar depth. Numerous large osteoblasts lie upon the osteoid zones, but in the more cellular part

of the strand beneath the periosteum the zones of osteoblasts are frequently interrupted by osteoclasts in Howship's lacunæ. The lacunæ almost invariably indent osteoid zones and not calcified bone. The junction of the fleshy segment with the bony is sinuous, with concavities towards the bone.

Remarks.—The changes in the bone are essentially similar to those in *Case* 1. Great resorption is associated with apposition. All the normal bone appears to have been resorbed except a few microscopic pieces near the medulla of the lower, bony, segment. Trabeculæ of woven coarse-fibred and intermediate bone have been formed. These are almost all very slender and seldom show more than one system. Active apposition is in great excess of active resorption. Except in the neighbourhood of areas of more active cellular proliferation in the marrow active resorption is seldom seen and is slight. A conspicuous feature is the occurrence of active apposition by osteoblasts upon trabeculæ which are undergoing active resorption by osteoclasts in Howship's lacunæ. The depth of the osteoid zones is within the limits of the zones in healing fractures in healthy adults. There is again, therefore, no evidence of osteomalacia. The fibrosis of the marrow is again closely associated with apposition and resorption. Near the medulla in the lower segment the fibrosis is incomplete, small areas of marrow being still adipose. The trabeculæ that abut upon these areas are, however, bordered by a zone of fibrosis. In general it can be said that the fibrous marrow is more cellular where conspicuous resorption accompanies apposition than where apposition is alone seen, and that there is no bone in the areas of most cellular, least differentiated, fibrous marrow.

Bone in the upper segment is confined to septa of fibrous marrow which separate rounded areas of a very cellular marrow rich in osteoclasts. The osteoclasts are not now eroding bone, and they are so numerous, large, and evenly distributed that it does not appear justifiable to attribute their presence to recent resorptive activity. These cellular areas have caused expansion of the bone. Histologically they cannot be differentiated from the less anaplastic examples in a series of osteogenetic myelomata, or osteoclastomata, removed from the ends of long bones in skeletons free from general changes. In a nomenclature depending upon morphology, therefore, such areas are entitled to the name 'osteoclastoma', although their retrogression following excision of enlarged parathyroid glands points to their not being autonomous neoplasms.—H. M. T.

FIG. 182.—*Case* 2. Generalized osteitis fibrosa. Tumour of right superior parathyroid body. (*Actual size.*)

2. Right Superior Parathyroid Body.—

MACROSCOPIC.—An oval body, measuring 2·3 × 1·5 × 0·9 cm. and weighing 1·3 grm. (*Fig.* 182). One surface was convex, the other slightly concave. Externally it was brown-yellow, even, and smooth except where a cord of areolar tissue was attached near one pole. The cut surface was homogeneous, moist, and paler brown-yellow. The cord of areolar tissue attached it to a mass (2 × 1·2 × 0·6 cm.) which was darker brown and had a slightly nodular surface. The cut surface was a considerably darker brown than that of the oval mass, and glistened conspicuously.

MICROSCOPIC.—The oval body is a parathyroid gland. It has a thin capsule of collagenous and elastic fibres, and is divided by a net of delicate collagenous

fibrils (Laidlaw's and van Gieson's stains) into small acini (*Fig.* 183). The interacinar septa contain capillaries, venous capillaries, or veins. Most of the acini are filled with mutually compressed cells, but a few have a central sphere of oxyphil coagulum surrounded by a row of cubical cells. Giant nuclei and multiple nuclei are conspicuous features. Most of the cells are completely dropsical or ballooned principal cells in which the cytoplasm is reduced to a basophil membrane. These measure from 7 to 23 μ in mean diameter. Most, however, are from 11 to 12 μ with a nucleus of 6 μ. In the larger forms the nuclei are from 6 to 19 μ, and some larger forms have two nuclei. Almost all the nuclei are deeply stained, but show a close net of chromatin, numerous nodes, and one to six nucleoli. In places are a few principal cells with a reticular basophil cytoplasm. They measure 7 to 13 μ, usually

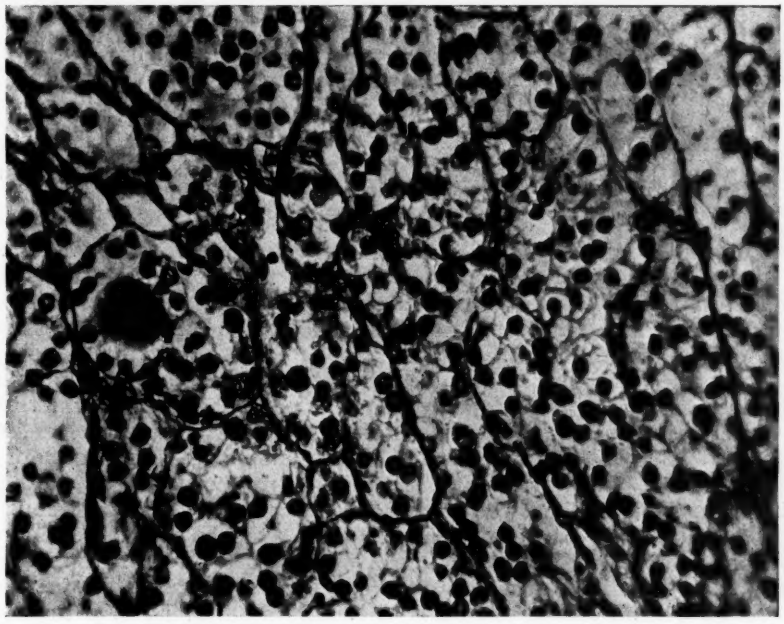

FIG. 183.—*Case* 2. Enlarged parathyroid gland. Generalized osteitis fibrosa. Acini containing ballooned principal cells; in one there is a lumen filled with coagulum. Laidlaw's collagen-reticulum silver stain. (× 320.)

9 to 10 μ. The nuclei average 6 μ and are either lightly or deeply stained. In those in which vesiculation is marked a pale oxyphil substance usually lies in the meshes of the remnant of basophil reticulum within a basophil membrane. One or two oxyphil cells are seen in each alveolus in one small area, but elsewhere they are very scanty. They are almost all of the pale oxyphil type with a basophil membrane. Most measure from 12 to 13 μ, with nuclei of 6 to 7 μ; but there are a very few small examples of 9·5 μ and several large forms up to 25 μ. The largest nucleus measures 8 μ, but several of the larger cells have two nuclei and one has four. Almost all the cells that surround coagulum are principal cells. Herxheimer's method shows one or two lightly stained spheres, up to 3 μ in diameter, within ballooned cells. Best's method shows abundant glycogen within the ballooned cells. It is sometimes present in scattered droplets, but more often fills the cell or forms a crescent in the periphery.

The body attached to the parathyroid gland consists chiefly of a rounded nodule of slightly fibrotic thyroid tissue. Almost all the acini contain a thin colloid and are bounded by a row of well-defined flattened cubical cells. A few acini are greatly distended with this colloid. A very few small acini are lined with larger ill-defined cells, and appear to be in an early stage of colloid secretion. There are a

few groups of lymphocytes, with occasional plasma cells, in lymphatic sinuses. This nodule is separated by a fibrous septum from a strip of thyroid tissue. The strip differs in that fibrosis is confined to the neighbourhood of the septum, distension with colloid is not so great, and there is only one minute area of lymphocytic infiltration.

Remarks.—The only abnormality in the parathyroid body besides enlargement is the presence of giant nuclei and multiple nuclei. The giant nuclei are numerous, and are very conspicuous under a low power. Giant and multiple nuclei are sometimes as conspicuous in the thyroid gland of Graves' disease. The appearances suggest an exceptional functional activity. The hyperplasia resembles that in *Case* 1 in that it consists chiefly of ballooned principal cells; these cells contain much glycogen. Oxyphil cells are, however, relatively much more scanty than in *Case* 1, and they are almost all of the pale variety. Further, the acini are smaller and more completely limited (*Fig.* 183).

If the portion of thyroid gland examined can be taken to represent the whole, the gland shows a greater activity than is normal at the age of the patient.—H. M. T.

Subsequent Progress.—Twenty-two hours after operation Chvostek sign was positive. On the second day tinglings occurred in the fingers, and the bones were found to be less tender on pressure. On the third day the patient complained of cramps in the fingers, hands, feet, and trunk, so that she felt 'tied in knots'. On the fourth day, and subsequently, passive movements of the limbs and pressure on the bones caused no pain. Immediately after operation a diet containing milk, ice-cream, and eggs was given, together with calcium lactate (5 grm. three times a day). In spite of the high calcium intake, cramps in the limbs persisted, and parathormone was given by intramuscular injection from the sixth day for twenty-six days (*Fig.* 179). Intramuscular calcium gluconate (10 c.c. of a 10 per cent solution) was used to relieve tetany, and on one occasion intravenous calcium chloride (10 c.c. of a 5 per cent solution) was required (*Fig.* 179). Irradiated ergosterol (one radiostol tablet twice a day) was given over a long period. On the tenth day after operation acuity of hearing became remarkably increased and remained so for five days; subsequently hearing was normal. All manifestations of tetany ceased on the seventeenth day after operation. On the nineteenth day she began to be alert and interested, and found that she could turn over the pages of a book. Five weeks after operation the bony tumour on the dorsum of the right hand had almost disappeared, and the swelling inside the mouth, corresponding to the tumour on the mandible, was much smaller. In six weeks, after treatment by massage, she was able to move her arms down to her sides. In eight weeks she was lifted into a chair and soon became accustomed to sit comfortably. Three months after operation normal menstruation occurred. Muscular development improved. Five months after operation she stood and began to walk with assistance. In seven months she began to knit, to sew, and to write. In nine months she walked with crutches and was soon able to use them to climb up and down a few steps. Ten months after operation the weight had increased by 24 lb. (6 st. 9 lb. on April 27, 1931).

Radiograms (Nov. 24, 1930).—Density of bone shadows, as compared with controls, is not appreciably different from what was seen before operation. Cyst-like areas expanding bone are smaller, especially in the third right metacarpal, and some of them appear to be filling in. Renal calculi unaltered.

Blood-count (May 4, 1931).—Red cells, 4,000,000; Hb., 50 per cent; C.I., 0·62; leucocytes, 8000; differential count, normal.

Urine (Dec. 2, 1930).—Acid; sp. gr., 1018; albumin, faint trace; no sugar; deposit, amorphous urates. The average daily output of urine (July–November, 1930) was 570 c.c.

Calcium and Phosphorus Metabolism after Operation.—After parathormone injections were discontinued the serum calcium remained slightly below the normal level, namely 9·0 mgrm. per 100 c.c., and the plasma phosphorus rose to above 2·0 mgrm. per 100 c.c. (*Fig.* 179). Latent tetany disappeared. The plasma phosphatase remained high, the average of 13 readings after operation being 0·73 mgrm. Four months after operation the calcium output was estimated for two three-day periods on a low calcium diet. The urinary output of calcium had dropped to half the pre-operative level, but was still twice that of the normal control (*Fig.* 180).

Remarks.—Gold (1928) was the first to demonstrate hyperparathyroidism in a case of generalized osteitis fibrosa, associated with multiple tumours and cysts of bone. Similar cases, in which bone tumours were obvious on clinical examination, have since been recorded (Barr, Bulger, and Dixon, 1929; Wilder, 1929). Renal calculi have often been demonstrated in hyperparathyroidism, and the present case shows that persistent slight albuminuria may be the only indication of their presence. Generalized osteitis fibrosa has sometimes been treated with irradiated ergosterol in the hope of increasing the apposition of bone (Regnier, 1929). In at least one case (Snapper and Boevé, 1931) good evidence has been obtained of the effect of such treatment in increasing the density of bone as judged by radiograms. In the present case no improvement occurred even with the prolonged use of large doses of cod-liver oil, irradiated ergosterol, and ultra-violet irradiation.

The remarkable improvement after removal of a parathyroid tumour is of great interest. The patient has been changed from a pain-racked bed-ridden cripple to an almost normal individual. We must not forget, however, that the urinary calcium output, as estimated four months after operation, was still in excess of the normal, and it is possible that hyperparathyroidism still exists and may even cause a return of symptoms. Decrease in size of osteoclastomata after removal of a parathyroid tumour was first recorded by Barr, Bulger, and Dixon in 1929. Restoration to normal of the menstrual function has also been previously recorded. The temporary occurrence of hyperacusis following the operation is of interest. It has been observed where the serum calcium was low from another cause.

Case 3.—**Hyperparathyroidism. Generalized osteitis fibrosa. Bilateral renal calculi.**

A. J. F., married woman, aged 49. (L.H. Reg. No. 41234/1930.)

History.—1919: Onset of thirst, dry mouth, and polyuria. Began to take two quarts of water or lemonade during the night.

1922.—Attack of symptomless hæmaturia, blood and pus found in the urine, bilateral renal calculi demonstrated in radiograms. Operation (Mr. F. S. Batchelor, Dunedin): right nephrotomy—removal of large renal calculus. Temporary relief of thirst. Three years after this operation began to have severe attacks of renal colic, which have persisted until the present time.

1927.—Became unable to walk long distances owing to fatigue. Noticed a hard lump on the right shin, which grew larger and became tender. Right leg stiff and painful, unable to climb steps. Pain around joints, for which all teeth were extracted. Operation (Mr. F. S. Batchelor): removal of portion of bone tumour for histological section. Report: "portion of bone from right tibia shows matrix of fibroblasts and threads of fibrous tissue, also fragments of osteoid tissue. Many osteoclasts are present in the matrix and applied to many of the osteoid fragments. There is also blood pigment from old hæmorrhages. The appearances

are those seen in the cystic areas of osteitis fibrosa cystica (von Recklinghausen's disease)."—Dr. Murray Drennan (Dunedin).

Following this operation outward bowing of the right thigh occurred. The patient wore a splint for two years, removing it when she went to bed. There was pain in the left hip and groin after walking any distance. Both legs became very tender, and at one time she could not bear anything to touch them. Radiograms of the bones were taken every three months, and she was told that some of the swellings in the bones disappeared, and fresh ones appeared elsewhere. Treatment with preparations of vitamin D and with ultra-violet irradiation had some good effect.

November, 1929.—Discarded caliper splint. Less pain in bones, still unable to mount stairs. Walked with a stick, but could manage half a mile with ease.

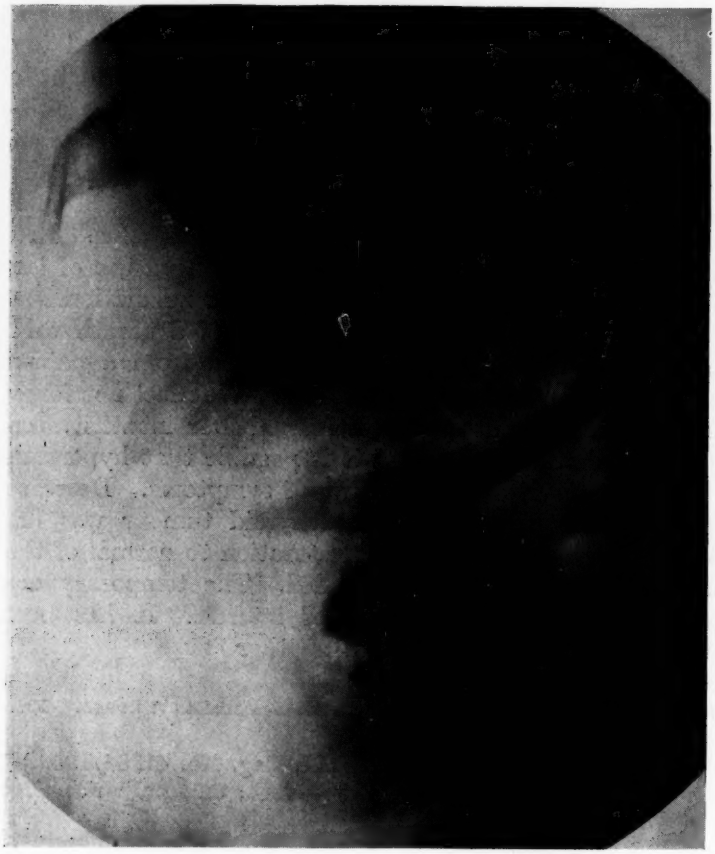

FIG. 184.—*Case* 3. Radiogram of right kidney.

Past History.—Onset of catamenia at 14; lasted five or six days; regular every month until a year ago, then suddenly ceased. Five children alive and well. One miscarriage at three months in 1918; stillborn child in 1919, at onset of first symptoms of illness. In each case labour was normal. Babies all breast-fed until nine months. For many years past had had repeated dental treatment; six teeth were crowned. There was no dental caries; the teeth were removed on the assumption that they caused rheumatism. Has never fractured a bone. No family history suggesting disease of bones.

Aug. 22, 1930.—Admitted to the London Hospital.

On Examination.—Height 5 ft. 4 in. Weight 9 stone. Well-nourished woman, gets about well, prefers to use a stick. Calvaria of normal size and contour. Sclerotics white. Pupils equal and regular, react to light and on accommodation. Right and left coronary cataract with some small scattered opacities in the anterior cortex (Mr. C. Goulden). Hearing normal. Double dentures. Tongue clean. Mucous membranes of normal colour. Small, firm adenoma 2·7 cm. diam. in lower pole of left lobe of thyroid gland. No other tumour felt in neck. Heart and lungs normal. Blood pressure 120/90 mm. mercury. No hypotonicity of muscles. No abnormality in nervous system. Trousseau and Chvostek signs absent. No tenderness on pressure upon shafts of bones. Slightly raised, hard, non-tender, bony swelling on inner aspect of right tibia 4 cm. diam., covered by scar of operation. Depression felt in subcutaneous surface of left tibia immediately below left knee-joint. No other bone deformities nor tumour. Nephrotomy scar in right loin.

Urine.—Acid; sp. gr., 1005; albumin, heavy cloud; no Bence Jones protein; deposit, leucocytes and red cells.

Blood.—Blood-count, bleeding time, and coagulation time normal. Wassermann reaction negative.

Fig. 185.—*Case* 3. Radiogram of skull.

Radiograms.—Bilateral renal calculi (*Fig.* 184). Pale, rounded cyst-like areas in lower end of right femur, both tibiæ, metacarpals, phalanges of fingers, bones of pelvis, and calvaria (*Fig.* 185). Slight diminution of density of shadows of bones as compared with a normal control.

Calcium and Phosphorus Metabolism before Operation.—Hypercalcæmia was constantly present, the serum calcium reaching as high as 15·0 mgrm. per 100 c.c. The plasma phosphorus was low, namely, 1·8 mgrm. per 100 c.c. (*Fig.* 186). Plasma phosphatase, 1·16 mgrm. For three three-day periods on a known low calcium intake the calcium output in the urine was approximately four times the normal, that in the fæces being normal (*Fig.* 180).

Operation (Mr. A. J. Walton—Aug. 29, 1930).—Under open ether anæsthesia

a collar incision was made in the neck. Small adenoma (2·7 cm. diam.) in lower pole of left lobe of thyroid gland. Behind this was a tumour 6·8 cm. long lying between the trachea and the œsophagus with its lower pole in the mediastinum. It was easily dislocated upwards, and was found to have a vascular pedicle attached to the inferior thyroid artery. The pedicle was ligatured and the tumour

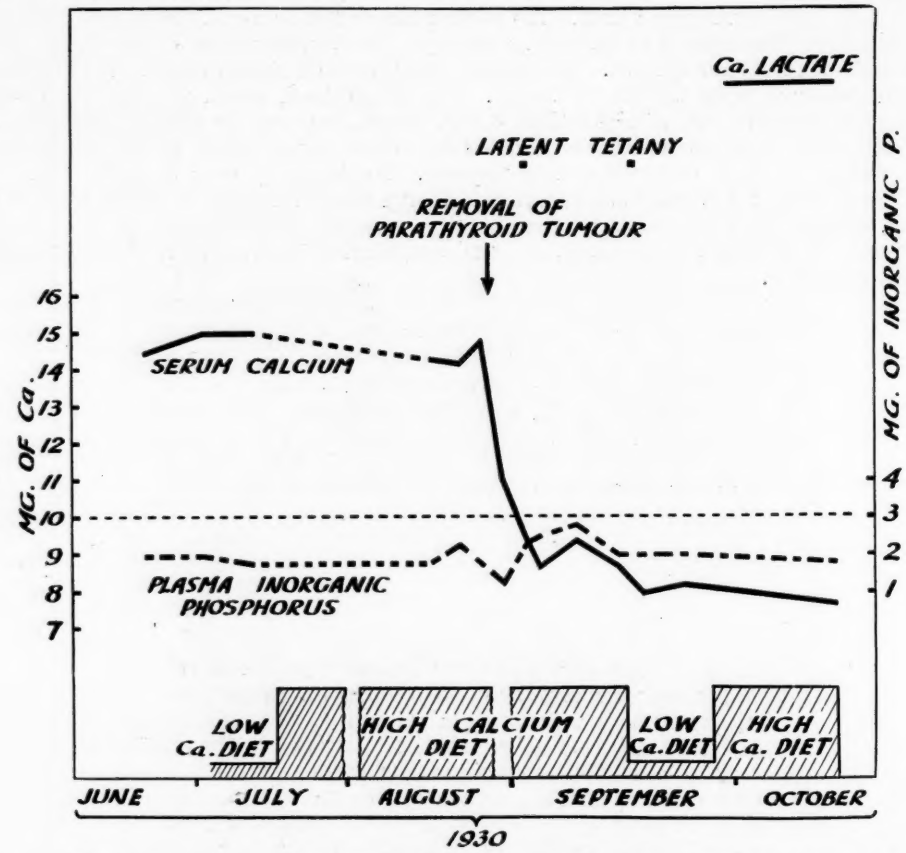

FIG. 186.—*Case* 3. Chemistry of the blood. The blood was examined at intervals for three months before and for two months after operation. The low calcium diet was that given during the investigation of the calcium balance. The high calcium diet was not weighed. It included four pints of milk daily, together with ice cream, cheese, and eggs.

removed. No other parathyroid bodies were disturbed. The adenoma was shelled out from the left lobe of the thyroid gland, which was then sutured. An incision was made over the bony tumour in the right tibia. A portion of tumour together with the corticalis below it was removed with the periosteum intact.

Pathological Report.

(PROFESSOR H. M. TURNBULL.)

Tissues removed at operation. (S.D. 2003/1930.)

1. Right Tibia.—

MACROSCOPIC.—The specimen was a vertical slice covered with periosteum and measuring 3·5 cm. long. The cut surface showed beneath the periosteum three successive kinds of tissue. In the upper 1·8 cm., which corresponded to the swelling seen upon the tibia, it was 0·7 cm. wide and was occupied by a soft tissue, which was

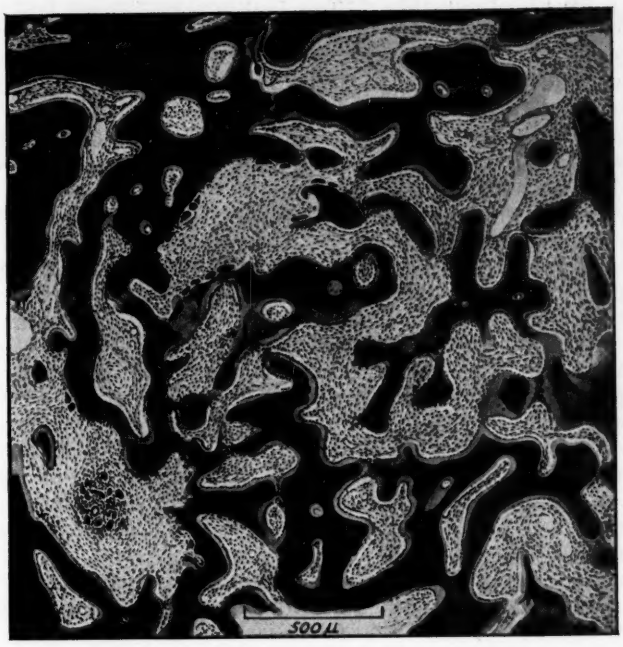

FIG. 187.—*Case* 3. Right tibia, central segment. Generalized osteitis fibrosa. Note the minute osteoclastoma, and compare the general changes with those in the example of focal osteitis fibrosa (*Fig.* 188). Müller's fluid followed by nitric acid; Weigert's iron-hæmatoxylin and van Gieson.

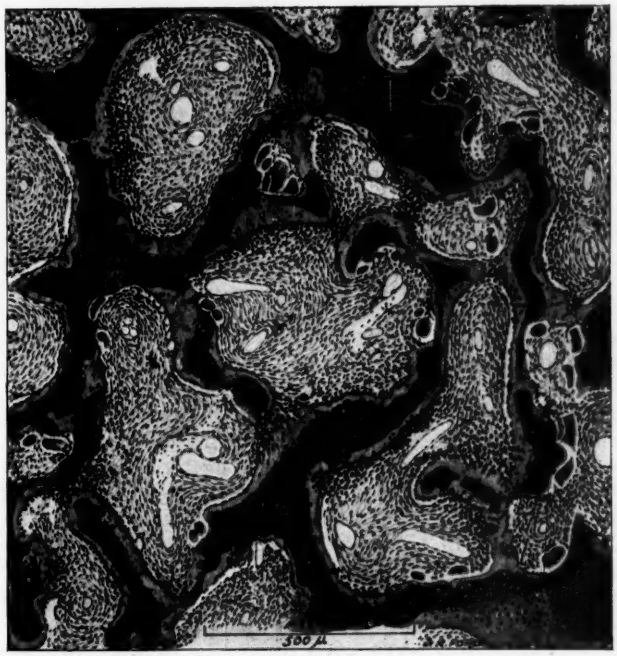

FIG. 188.—*Case* 8. Right femur. Osteitis fibrosa in multiple foci. Müller's fluid, followed by nitric acid; Weigert's iron-hæmatoxylin and van Gieson.

mottled grey-brown and mahogany-brown and was separated from the periosteum by a very thin interrupted sheet of gritty bone. The central 1·1 cm. was also 0·7 cm. wide, could be cut without difficulty with a knife, and showed a close meshwork of delicate trabeculæ of bone enclosing yellow-brown tissue. The lower 0·6 cm. was 0·5 cm. wide and consisted of a grey bone which differed from ivory bone only in being stippled with dark points. The edge of this dense bone where it met the spongy was concave and sharply defined. The junction of the spongy bone with the soft tissue was sinuous and less sharply defined.

MICROSCOPIC.—The bone was fully decalcified in Müller's solution followed by nitric acid. In the lower of the three segments described above the outer two-thirds of the corticalis are abnormal only in that there are many small medullary spaces throughout and a few bays in the periosteal surface, which communicate with medullary spaces. The bone consists of systems of lamellar bone which enclose areas and systems of woven bone. Active resorption is shown by numerous osteoclasts in Howship's lacunæ in the margins of some of the medullary spaces. Active apposition preponderates, however, most of the medullary spaces being lined with an osteoid zone covered by closely-packed large osteoblasts. The medullary spaces contain a fibrous marrow. In the inner third of the corticalis the bone is reduced to a few narrow trabeculæ, which lie in a fibrous marrow that surrounds a small rounded osteoclastoma. The trabeculæ are undergoing active resorption and apposition. The latter predominates and has led to the formation of some small processes of woven bone.

In the central segment (*Fig.* 187) the medullary spaces in the outer two-thirds of the corticalis are larger and have anastomosed so that the compacta is converted into a finely meshed spongiosa. The medullary spaces are of very irregular shape. Their longer axis is most often at right angles to the long axis of the bone. In some fields the bone is in slight excess of the soft tissue, in others the soft tissue is in great excess. In one of the larger medullary spaces is a minute osteoclastoma (*Fig.* 187). The trabeculæ consist chiefly of lamellar bone, but this encloses numerous areas and systems of woven bone. Similar woven bone has been formed in places immediately beneath a stout tendinous insertion upon the outer surface, and the inclusions beneath doubtless represent periosteal interstitial systems that have been incorporated in the growth of the original compacta. Active apposition is present almost throughout and is in great excess of resorption, but numerous osteoclasts in lacunæ are present in a few places. The medullary spaces contain a fibrous marrow. In the inner third of the corticalis the bone is again reduced to a few scattered slender trabeculæ in a zone of fibrous marrow which surrounds two osteoclastomata.

In the upper segment the corticalis is reduced to a few trabeculæ of very irregular shape. These lie in a fibrous marrow that forms septa between, and to a less extent within, large rounded osteoclastomata and also separates the osteoclastomata in places from the periosteum. Most of the trabeculæ consist of lamellar bone, but towards the osteoclastomata are a few very slender trabeculæ of recently formed woven bone. Active resorption is shown by many osteoclasts in lacunæ in osteoid tissue or in bone, but active apposition is again in great excess.

In all segments the osteoid zones are deep. They appear to increase in depth the more the corticalis has been eroded. This apparent increase in depth is due to tangential section being ever more frequent the more irregular the outline of the trabeculæ. Where the zones are cut at right angles to their surface the depth is within the limits of that found in actively healing fractures. The fibrous marrow is similar to that described in other specimens. It varies slightly in density. The less dense areas contain very wide capillaries, and lie chiefly near the large osteoclastomata. Cells loaded with iron-pigment are numerous throughout; they form dense masses near the osteoclastomata. The rounded areas called osteoclastomata are very similar to those that have been described in *Case* 2. They differ in that there is very great extravasation of red corpuscles within them and immediately round them.

Remarks.—A great resorption of bone is associated with a fibrotic marrow that contains osteoclastomata—that is to say, areas of greater cellularity containing great numbers of large osteoclasts. In the osteoclastomata there is no bone, in the fibrotic marrow at the margins of the osteoclastomata the corticalis has been reduced to a few slender trabeculæ. Farther from the osteoclastomata there is a porosity of the compacta, which is very great near the group of larger osteoclastomata but becomes less at a distance. Resorption of bone, therefore, has been very great and has caused the main change in structure. Lacunar resorption is still active in places, but apposition of bone is now the predominant activity. The apposition is taking place rapidly and the osteoid zones are correspondingly deep, but there is no evidence of a delay in calcification such as occurs in rickets and osteomalacia. This case differs from the first two in that most of the bone present, and almost all where the porosity is least, appears to be a remnant of the original, normal compacta. The abnormal processes seen in the first two cases are here in an earlier stage.—H. M. T.

2. Left Inferior Parathyroid Gland.—

Macroscopic (*Fig.* 189).—The specimen was spindle-shaped, with one convex and one slightly concave surface, measured 6·8 × 2·8 × 1·4 cm., and weighed 13·5 grm. The outer surface showed a few, irregularly scattered shallow sulci, in one of which blood-vessels entered the gland. It was covered with a transparent capsule. In about one half of the cut surface a homogeneous yellow-brown tissue enclosed a few well-defined cysts (from 0·2 to 1 cm. in diameter), containing clear fluid. In the other half the yellow-brown tissue was ragged and spongy owing to numerous cysts with ill-defined, irregular boundaries.

Fig. 189.—*Case* 3. Generalized osteitis fibrosa. Tumour of left inferior parathyroid body. (*Actual size.*)

Microscopic. — The gland is surrounded by a thin sheet of collagenous and elastic fibres, and is imperfectly divided into acini by numerous capillaries or larger vessels sheathed by collagenous fibrils. No other reticulum is shown by Laidlaw's silver impregnation. In three of the six portions taken for microscopic examination there are a few small acini of principal cells immediately under the capsule. The cells measure from 7 to 9 μ in mean diameter. They have a basophil reticular cytoplasm, no visible cell-membrane, and a nucleus of 4 to 5 μ, which is usually deeply stained. All the rest of the gland is occupied by oxyphil cells. These are almost all pale oxyphil cells (*Fig.* 190). They measure from 9 to 19 μ, but most are 14 to 15 μ. They are polygonal from mutual compression, and their basophil cell-membranes form a conspicuous polygonal intercellular net. The oxyphil cytoplasmic granules are set closely in some cells, but in the majority they are unusually wide apart, many cells having a very dropsical appearance. The nuclei measure from 4·5 to 6 μ, are usually lightly stained, and occasionally show one or two inconspicuous nucleoli. Lysis, accompanied by shrinkage, of nuclei is frequent; one

karyokinetic figure was seen. Dark oxyphil cells are scanty, but lie here and there, compressed between pale oxyphil cells. They measure from 6·5 to 8·5 μ, and have a nucleus of 4 to 4·5 μ. The nuclei are deeply stained, and usually narrow-oval. In tissue fixed in alcohol and stained by Best's method almost all the pale oxyphil cells contain glycogen. The glycogen is usually in the form of small granules scattered throughout the cell, but many cells contain larger droplets and irregular masses, which usually lie near the periphery of the cell, often forming

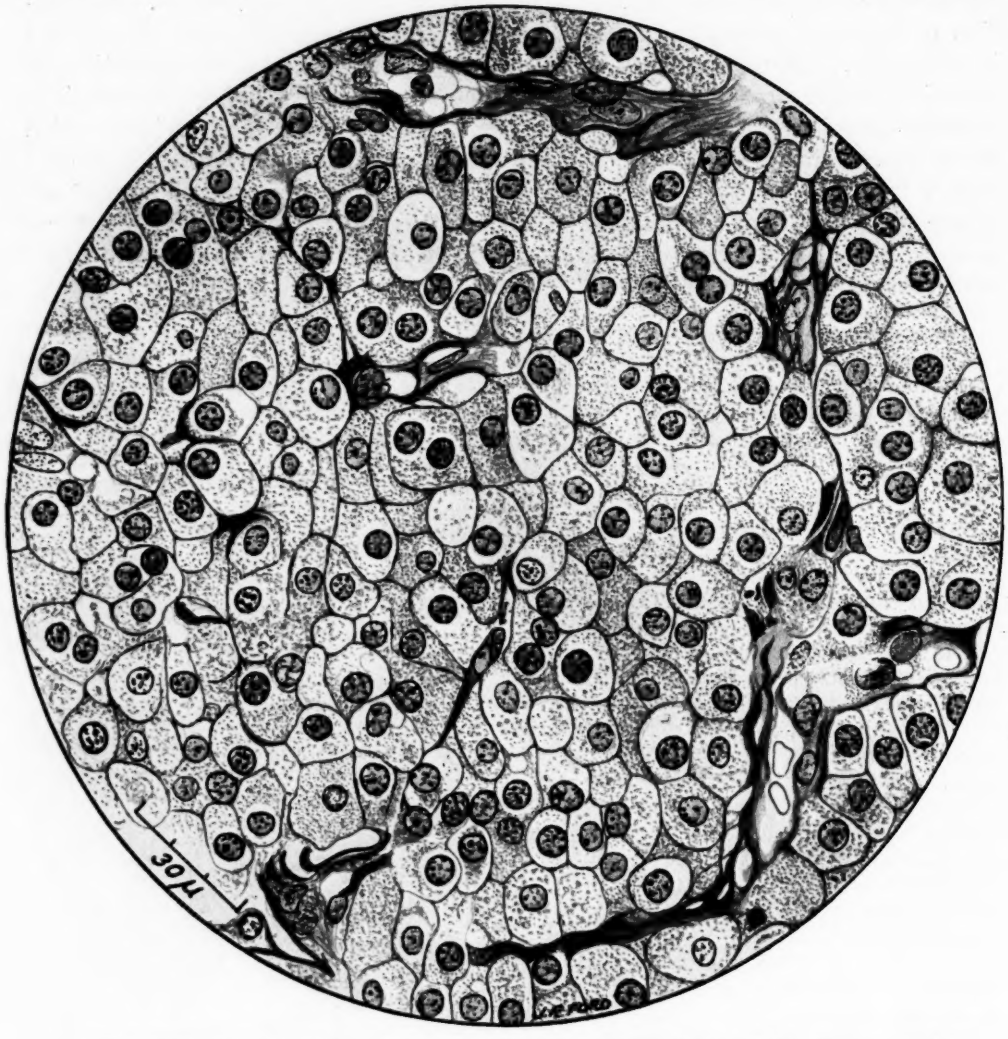

FIG. 190.—*Case* 3. Enlarged parathyroid gland. Generalized osteitis fibrosa. Pale oxyphil cells, with granules separated to various degrees by dropsy. Weigert's iron-hæmatoxylin and van Gieson.

a crescent within the cell membrane. Glycogen is, therefore, very abundant, but does not fill these cells so completely as it fills the ballooned principal cells of *Case* 2. No fat is shown by Herxheimer's method, but many cells contain very lightly stained refractile granules similar to, but usually much smaller than, those seen in previous cases. From their size and position they appear to be granules of glycogen that have survived fixation in formaldehyde. Even in the more solid parts of the gland there are a few clefts or larger cystic spaces within the acini.

In the spongy parts such cysts are very numerous and are often of large size. The number of cells in the walls of the cysts usually varies in different parts of the circumference. The inner margin of the smaller cysts is irregular, in the larger it is even. The cysts contain a thin oxyphil, usually bubbly coagulum, in which there are occasionally degenerated epithelial cells and rarely a few red corpuscles. Droplets of glycogen are occasionally present, chiefly within degenerated cells. The vascular septa are occasionally distended by a similar coagulum; more often they are distended by œdema. Within the septa are a few tissue-mast-cells; a few lymphocytes and one or two plasma cells were also found.

3. A Body Excised from Lower Pole of Left Lobe of Thyroid Gland.—

Macroscopic and Microscopic.—A spherical, encapsulated colloidal adenoma of the thyroid gland, showing cystic and atheromatous degeneration and extensive hyaline fibrosis. It measured 2·7 cm. in diameter, and weighed 8·8 grm.

Remarks.—In the enlarged parathyroid body the cells and their arrangement are in no way atypical. The appearances suggest a hyperplasia and excessive secretory activity rather than an autonomous neoplasm. Here and there beneath the capsule are a few small acini containing principal cells. All the rest of the gland is occupied by oxyphil cells. The enlargement contrasts, therefore, sharply with that of *Case* 2, which consisted almost entirely of principal cells, and less sharply with that of *Case* 1, in which oxyphil cells took a relatively small, though actually large, share. Here, however, unlike *Case* 1, the oxyphil cells are almost all of the pale variety, and in general they show much dropsical separation of the oxyphil granules (*Fig.* 190). They contain much glycogen, but are not so filled with glycogen as the ballooned principal cells of *Case* 2. Cystic spaces filled with thin oxyphil secretion are very numerous, and this secretion also infiltrates the septa in places.—H. M. T.

Subsequent Progress.—On the first day after operation the patient complained of feelings of pins and needles in the hands. No manifest tetany occurred. Trousseau sign was negative and Chvostek sign was only twice elicited. On the fifth day after operation the serum calcium dropped to 8·7 mgrm. per 100 c.c. (*Fig.* 186). At this time she was feeling well, thirst had completely disappeared, and there was no longer any aching in the limbs. Radiograms of the kidneys showed no change in the shadows of the renal calculi. Ten months after operation the patient was perfectly well, had gained 2 st. 9 lb. in weight, and could walk four miles without fatigue. Thirst and aching in the bones had disappeared.

Calcium and Phosphorus Metabolism after Operation.—A diet high in calcium content was resumed after operation; 15 grm. of calcium lactate were given daily. Intramuscular calcium gluconate and parathormone injections were unnecessary. Three weeks after operation the calcium output was estimated for three three-day periods on the same low calcium diet as before. The output in the urine was very much less than in a normal individual; that in the fæces was normal (*Fig.* 180). Four weeks after operation the plasma phosphatase was 1·2 mgrm. Ten months after operation the serum calcium was 10·6 mgrm. per 100 c.c., and the plasma phosphorus 3·8 mgrm. per 100 c.c.

Remarks.—The spontaneous remission recorded in this case suggests that hyperparathyroidism may sometimes show relapses and remissions analogous to those seen in acromegaly and exophthalmic goitre.

Where four times the normal amount of calcium is excreted in the urine it is not surprising to find polyuria. Thirst and polyuria are mentioned in

five published cases of hyperparathyroidism. Both symptoms are usually promptly abolished after removal of the parathyroid tumour (Boyd, Milgram, and Stearns, 1929; Pemberton and Geddie, 1930). Some authors refer to the polydipsia and polyuria as diabetes insipidus (Rosenbach and Disqué, 1930).

Renal calculi have been recorded in ten cases, and renal colic was the presenting symptom in at least one case (Léri, Layani, Lièvre, and Weill, 1930). In one case renal calculi began to break up a few weeks after operation and were passed into the bladder (Hurst and Cosin, 1930).

Case 4.—**Hyperparathyroidism. Generalized osteitis fibrosa with multiple osteoclastomata. Otosclerosis.**

B. Y., married woman, aged 51. (L.H. Reg. No. 41770/1930.)

HISTORY.—1892: Acute febrile illness with severe pain in left hip followed by formation of an abscess which discharged profusely.

1893.—Painless swelling on upper part of right arm; discharge of pus and sequestrum.

1894.—Operation upon left hip for scraping of bone. Wound healed temporarily.

1895.—First noticed deafness. No pain. No otorrhœa.

1896.—Swelling of right hip resulting in formation of a sinus.

1901.—Dr. O. Amreim (Arosa) performed "exploration and curettage of the left iliac bone. A guinea-pig was inoculated with pus from the carious bone. Tuberculosis followed in the guinea-pig, and from these lesions tubercle bacilli were grown in almost pure culture." The sinus closed and only opened once again for a short time twelve years later.

1902.—Right sinus closed, was able to lead an active life, played tennis and hockey.

1915.—Pain in right ear. Tinnitus. High notes heard more easily than low notes. Swelling appeared over outer aspect of right orbit.

1919.—Infected tonsils removed.

1925.—Prolonged dental treatment for abscesses at apices of teeth.

1926.—Lump appeared in lower jaw and projected into right side of mouth. It was thought to be a dental cyst. Jaw became stiff.

October, 1926.—Mr. F. Barnes (Birmingham) removed portion of mass in mouth for histological section. Professor H. Wilson (Birmingham) reported, "the tumour has the structure of a 'myeloid sarcoma'. The stroma is fairly cellular and many of the giant cells are rather degenerate in appearance, but there is nothing to suggest that the growth is more malignant than is usually the case in such tumours. From the histological point of view the condition is definitely neoplastic, and the appearances cannot be explained on the basis of bone absorption or of any inflammatory process." Tumour removed from lower jaw through incision in skin.

April, 1927.—Swelling in jaw reappeared. Further operation for local recurrence of myeloma.

August.—Firm swelling in left upper jaw.

December.—Diplopia and dim vision in left eye. Professor A. Vogt (Zürich) found that "the left optic disc was definitely paler than the right. Incipient optic atrophy. The right fundus was normal. There was weakness of the left superior rectus oculi, and slight sensory loss in the area of the first branch of the left fifth cranial nerve."

January, 1928.—Could not recognize objects with left eye, but could appreciate light and dark. She was told that the tumour in the left upper jaw was a myeloma and that the defective vision was due to another myeloma. Professor P. Clairmont (Zürich) found "in the left post-nasal space arising from the left superior maxilla, a dark red swelling. It was explored and histological sections showed it to be a benign giant-celled tumour."

April.—Was told that she had optic neuritis due to pus behind left eye. Drainage of suppurative ethmoiditis by Mr. E. M. Woodman (Birmingham). Eyesight gradually improved. All bones now rather tender, so that even shaking hands was painful. Left hip very painful. Lump appeared in left thigh. Treated for rheumatism. Pain became worse. Radiogram showed large myeloma of left ilium.

June.—Following deep X-ray therapy for relief of pain she collapsed. Vomiting persisted for four days. Dr. E. M. Knott (Sutton Coldfield) called in consultation Dr. A. P. Thomson (Birmingham). Intravenous glucose was given.

December.—Recurrence of pain in left hip. At this time could hardly lift herself in bed. Deep X-ray therapy was repeated.

1929.—Other swellings appeared upon right thigh, left thigh, and lower part of right shin. These were not so painful as the previous ones.

July, 1930.—Dr. A. P. Thomson diagnosed hyperparathyroidism and confirmed this by an estimation of the serum calcium, which was found to be 13·8 mgrm. per 100 c.c.

Past History.—No history of rickets or tetany. Has never fractured a bone. No family history suggesting disease of bones. Catamenia commenced at age of 15; regular but rather excessive, lasting five to six days and coming on every three weeks. They ceased two and a half years ago. Had one miscarriage and then two normal pregnancies. Labours were difficult, requiring an anæsthetic and instruments. On the advice of her doctor her children were not breast-fed. Teeth were good until the age of forty, when she was found by X rays to have apical abscesses. The teeth were not affected by the pregnancies. Deafness has progressed during the last four years. One brother is very deaf, the condition dating from the age of 20. In 1929 was told she had a cataract in the left eye. Mother and two older sisters have cataracts. Always has a furred tongue. Certain articles of food cause nausea. Vomiting readily occurs after meals. No abdominal pain. No history of having passed gravel or stone. No increased frequency of micturition. Albumin has been present in the urine for some time.

Nov. 18, 1930.—Admitted to the London Hospital.

On Examination.—Height, 5 ft. 2 in. Weight, 7 st. 8 lb. Well-nourished woman, gets about well with crutches. Hearing very poor. Better in noisy surroundings. Uses instrument for right ear. Eustachian tubes patent. Tympanic membranes normal. Weber test: louder on right side. Rinné test: bone conduction equal on both sides. Air conduction: right better than left, but much poorer than bone conduction (Mr. N. Patterson). Calvaria, normal size and contour. Sclerotics white. R.V. 6/18. L.V. less than 6/60. Extensive senile changes in the lenses of both eyes. Cataracta coronaria, water clefts, cataracta cuneiformis. Powdery cataract in concentric layers. Left primary optic atrophy, right optic disc normal (Mr. C. Goulden). Double dentures. Caries of two of six remaining teeth. Tongue slightly coated. Mucous membranes normal colour. Thyroid gland normal. No tumour felt in neck. No hypotonicity of muscles. No abnormality in nervous system. Trousseau and Chvostek signs absent. Small bony swelling on outer aspect of right orbit. Three faint scars of operation—left orbit, left superior maxilla, and right side of mandible. No abnormality of spine or bones of thorax. Scar of old sinus over centre of shaft of right humerus. No abnormality of bones of upper limbs. Operation scar on left buttock, scar of old sinus on right buttock. 2 cm. shortening of left lower limb. Slight diffuse prominence of subcutaneous surface of right tibia in its middle third. Pressure upon the bones gives rise to no pain. Heart, lungs, and abdomen normal. Blood-pressure 160/100 mm. mercury.

Urine.—Acid; sp. gr., 1016; albumin, 1/20 volume; Bence Jones protein absent; no sugar; deposit of epithelial cells. Blood-urea, 0·033 per cent.

Blood-count.—Red cells, 4,600,000; Hb., 60 per cent; C.I., 0·65; leucocytes, 5000; differential count, normal. Bleeding time and coagulation time, normal. Wassermann reaction negative.

Radiograms of Bones.—Cyst-like area in upper part of shaft of right femur

expanding corticalis in region of great trochanter. Similar area in left ilium adjoining acetabulum. Ankylosis and deformity of left sacro-iliac synchondrosis, evidently a change of long standing. By contrast with the bones of a control subject the right tibia and fibula (*Fig.* 191), left hand and forearm, as well as other bones, show slight but definite diminution of density. No fractures nor other deformity. Calvaria is mottled and shows three rounded pale areas in the frontal region, the largest more than 1 cm. in diameter; the tables are not thickened.

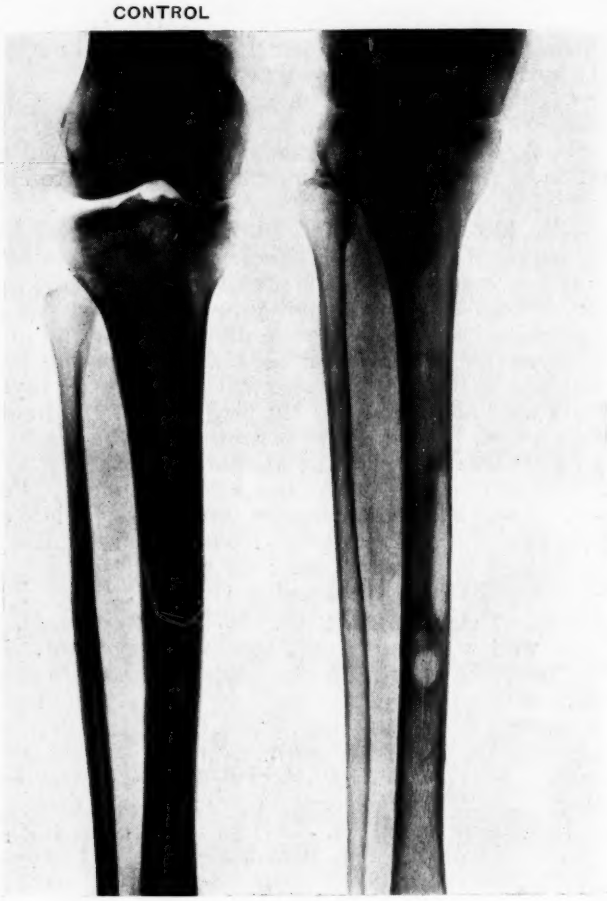

FIG. 191.—*Case* 4. Controlled radiogram of right tibia and fibula.

Radiograms of Kidneys.—Kidney shadows normal in size. Group of small calculi (largest 3 mm. diam.) seen in region of each kidney.

Calcium and Phosphorus Metabolism before Operation.—During the five months preceding operation the serum calcium varied between 12 and 15 mgrm. per 100 c.c., and the plasma phosphorus was only once above 2·0 mgrm. per 100 c.c. (*Fig.* 192). Plasma phosphatase 1·06 mgrm. The calcium output was estimated in the urine and fæces for one three-day period, the patient being kept on a weighed diet of known low calcium content. The calcium output in the urine was about 50 per cent greater than in the normal control, that in the fæces being almost the same as in the control (*Fig.* 180).

FIRST OPERATION (Mr. A. J. Walton—Nov. 26, 1930).—Under open ether anæsthesia. Collar incision made in neck. The sternomastoid muscles were retracted and the pretracheal muscles divided. Right and left superior parathyroid

bodies were identified and were normal. No tumour felt in neck on either side of trachea, even on passing the finger 3 cm. into the thorax. Inferior pole of right lobe of thyroid gland was paler and firmer than the rest of the thyroid tissue. This was evidently due to a tumour which did not, however, alter the normal contour of the thyroid gland. The thyroid gland was incised over the tumour and

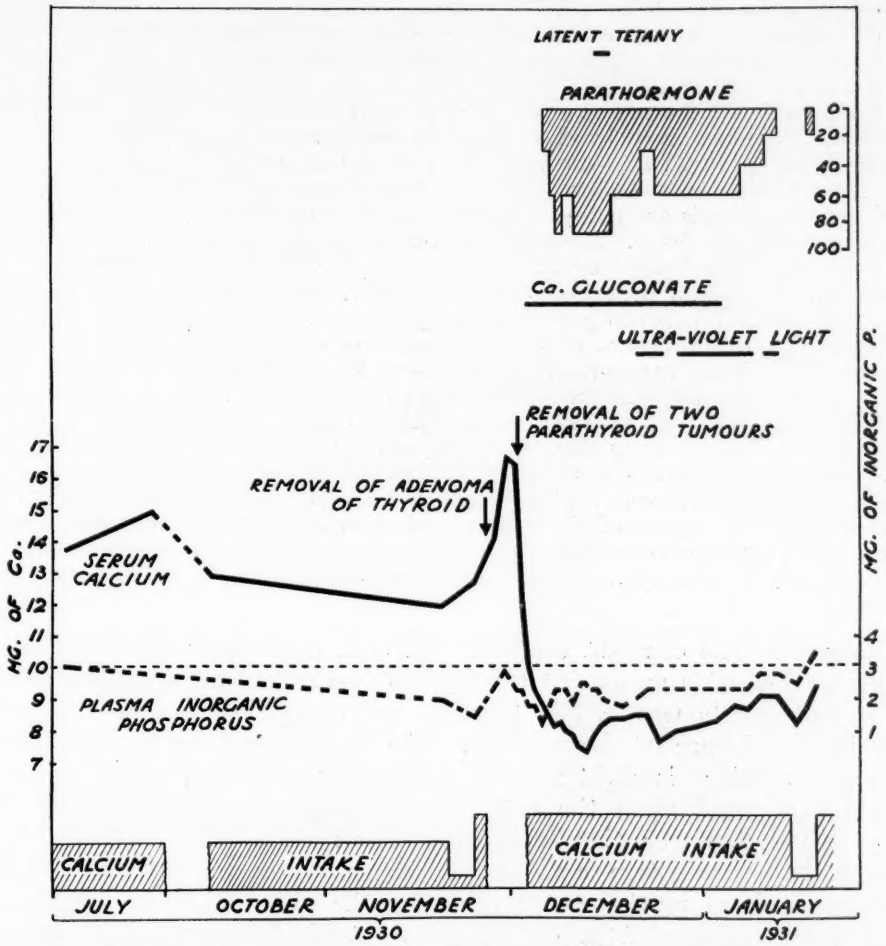

FIG. 192.—*Case* 4. Chemistry of the blood. The blood was examined at intervals for five months before and for two months after operation. The low calcium diet was that given during the investigation of the calcium balance. The high calcium diet was not weighed. It included four pints of milk daily, together with ice cream, cheese, and eggs. The scale indicating the dosage of parathormone represents units per day. The dosage of calcium gluconate was 10 c.c. of a 10 per cent solution daily, given by intramuscular injection.

an opaque yellowish-white swelling 2·0 by 1·5 cm. was shelled out (*Fig.* 193). The cut surface was glistening, firm, granular, and gritty. The thyroid gland was sutured and the wound

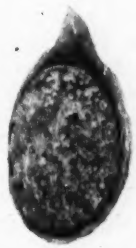

FIG. 193.—*Case* 4. Generalized osteitis fibrosa. Calcified adenoma removed at first operation from lower pole of right lobe of thyroid gland. (*Actual size.*)

closed. A piece of bone was removed from the corticalis of the right tibia immediately above the swelling. Chiselling was found difficult.

Pathological Report.

(PROFESSOR H. M. TURNBULL.)

Tissues removed at first operation. (S.D. 2731/1930.)

1. Right Tibia.—

MACROSCOPIC.—A longitudinal strip of bone covered with periosteum, 5·5 cm. long, 1 cm. wide, and 0·6 cm. deep. A fresh longitudinal section through the centre showed a pearly corticalis (2 mm. deep) in which many short longitudinal red streaks were just visible to the naked eye. This merged into a gelatinous, pale yellow, rarely red, tissue traversed by some thin sheet-like trabeculæ of bone.

MICROSCOPIC (*Fig.* 194).—Beneath the periosteum are a few bays in the bone, and some of these communicate with medullary spaces beneath. In the outer 2 mm. of the corticalis are many medullary spaces, which run for the most part in the long axis of the bone. Some of the larger intercommunicate. These spaces have evidently been formed by the widening of Haversian canals, of which very few remain. The outer contain a delicate, cellular fibrous marrow. In the inner the fibrous marrow encloses groups of adipose cells. The vessels are wide and engorged. The inner 4 mm. of the corticalis are represented by a few slender trabeculæ in adipose marrow. In a few bays in these trabeculæ, where there is active resorption by osteoclasts, the marrow is fibrous. There is much recent hæmorrhage in the adipose marrow, doubtless caused by the operation. The bone consists of lamellar systems enclosing several interstitial systems of woven bone. Resorption is shown in many places by single osteoclasts or groups of osteoclasts in Howship's lacunæ. At the extremities of a few medullary spaces the bone has a very gnawed appearance. Active apposition is shown by numerous osteoid zones covered by large osteoblasts, and is at present in excess of active resorption. The depth of the osteoid zones is within the limits of those in healthy young children.

Remarks.—The compact corticalis has been extensively converted into a spongy bone of wide mesh. At the time of removal of the specimen resorption by osteoclasts was still in progress but apposition was more general. There is no evidence of osteomalacia. The appearances are those of severe osteoporosis. There is slight fibrosis of the marrow focally, and this fibrosis appears to depend upon the activity of resorption and apposition. The picture is not, however, that of frank osteitis fibrosa. The portion of bone removed for examination came from the relatively healthy part of the skeleton. It is of much greater value for the differentiation of a case of diffuse osteitis fibrosa from one of focal osteitis fibrosa than an area of severe change.

2. Body Removed from Lower Pole of Right Lobe of Thyroid Gland.—

MACROSCOPIC.—An oval body measuring 2 × 1·5 × 1·1 cm. and surrounded by a zone of thyroid gland from 1 to 5 mm. thick. On section it felt gritty. The cut surface showed numerous chalky white rounded and rosette-like nodules, closely packed in a gelatinous grey tissue. The body was sharply defined from the thyroid tissue by a very thin transparent capsule.

MICROSCOPIC.—Portions decalcified in nitric acid and cut upon the freezing microtome and portions decalcified in Müller's solution and embedded in paraffin showed the nodule to be an extensively calcified colloid adenoma of the thyroid gland.—H. M. T.

PROGRESS AFTER FIRST OPERATION.—The patient remained fairly comfortable. No tinglings in fingers. No tetany. Trousseau and Chvostek signs negative. Twenty-four hours after operation the serum calcium was 14·1 mgrm. per 100 c.c.,

FIG. 194.—*Case* 4. Right tibia; corticalis. Generalized osteitis fibrosa. Note the extreme porosity; fibrosis is focal, and confined to Haversian spaces in the outer part of the corticalis. Müller's fluid followed by nitric acid; Weigert's iron-hæmatoxylin and van Gieson.

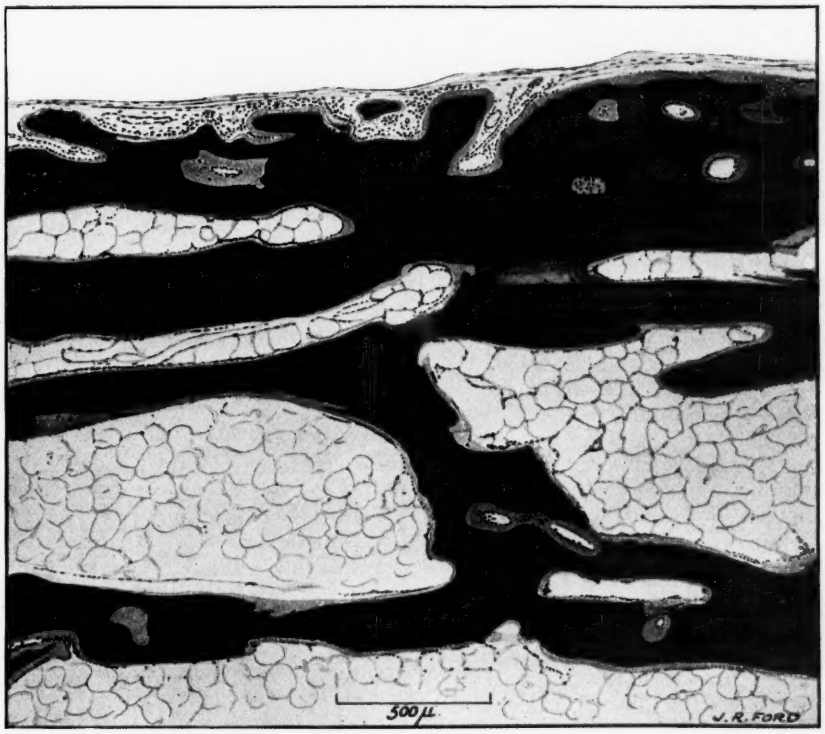

FIG. 195.—*Case* 9. Tibia; corticalis. Osteomalacia and osteoporosis. The osteoid zones are seen as pale seams upon the deeply stained, calcified bone. The porosity is shown by the compacta having become almost a spongiosa. Müller's fluid followed by nitric acid; Ehrlich's hæmatoxylin and eosin.

and the plasma phosphorus 2·3 mgrm. per 100 c.c. On the third day after operation the serum calcium was 16·7 mgrm. per 100 c.c. (*Fig.* 192). It was therefore concluded that the tumour removed was not of parathyroid origin. This view was confirmed when portions of the tumour decalcified in nitric acid and cut upon the freezing microtome showed the nodule to be an extensively calcified colloid adenoma of the thyroid.

Second Operation (Mr. A. J. Walton—Dec. 1, 1930).—Open ether anæsthesia. Stitches removed from old collar incision. Flaps reflected. Incision enlarged on both sides as far as upper border of thyroid cartilage. Carotid arteries exposed. Finger passed up on right and left sides as far as hyoid bone. No tumour found. Further incision along anterior border of left sternomastoid muscle to suprasternal notch. Right superior parathyroid body, measuring 2 × 1·3 × 1·2 cm. and situated deep to the œsophagus opposite the middle of the thyroid gland, was mistaken for a lymphatic gland and removed. Right inferior parathyroid body measuring 7·5 × 5·0 × 1·8 cm. was found behind trachea and œsophagus, opposite the bodies of the first and second thoracic vertebræ, well below the level of the clavicles. The inferior thyroid artery was divided and a finger inserted along the inner border of the longus colli muscle to reach the tumour. It was then displaced upwards and the pedicle to the inferior thyroid artery divided. The wound was closed in layers, and one drainage tube inserted.

Pathological Report.

(Professor H. M. Turnbull.)

Tissues removed at second operation. (S.D. 2778/1930.)

1, 2. **Right Parathyroid Bodies.**—

Macroscopic.—

1. *Larger Right Parathyroid Body* (*Fig.* 196).—The body was of elongated heart shape, with two small upward projections from the base and a bulge followed by a constriction on the left border. It measured 7·5 × 5 × 1·8 cm., and weighed 26·2 grm. It felt soft but elastic. The anterior surface was convex; the posterior was slightly concave from side to side. Portions of a thin sheet of blood-stained areolar tissue were easily removed. Between the two projections from the base a large vein lay posteriorly, and divided into a large right, large left, and a smaller median branch upon the posterior surface. Otherwise the outer surface was perfectly smooth. The posterior surface showed an area the size of a pin-head and a smaller area of opaque yellow. Cholesterin plates with notched angles were removed from these with a needle. The rest of the surface was of café au lait colour. The cut surface was soft, wet, elastic, very finely granular under a hand-lens, and of the same colour. It showed two small clefts filled with clear fluid.

2. *Smaller Right Parathyroid Body* (*Fig.* 196).—This measured 2 × 1·3 × 1·2 cm. It felt firmer than the large body and externally was of a slightly lighter yellow. On section it showed a large, round, bulging, grey-purple area (0·7 cm. in diameter) and several small purple areas in a yellow ground.

Microscopic.—

1. *Larger Right Parathyroid Body.*—The gland is surrounded by a thin capsule of collagenous and elastic fibres. It contains a few veins and is divided into small polygonal and rounded acini by the collagenous walls of capillaries (van Gieson's and Laidlaw's stains). In a few places the interacinar septa are wider, occasionally being hyaline but usually being either considerably or extremely rarefied by œdema. The cells are polygonal except where they border upon alveolar lumina. They are separated by a net of cell-membranes. Most of the cells measure from 10 to 12 μ and have nuclei of 5 μ. In some the cytoplasm appears dense but shows small triangular clefts and often a larger round vacuole; in most the cytoplasm consists of closely packed small granules. Scattered among these smaller cells and also occupying completely a few small areas are larger cells of 13 to 20 μ with nuclei of 5 to 6·5 μ, rarely 9 μ. Their cytoplasm consists of granules set farther

apart, and is sometimes interrupted by round or irregular vacuoles. The cytoplasm in all cells is oxyphil, and in all save the large cells is more oxyphil than is usual in pale oxyphil cells, The polygonal net of cell membranes is basophil. In sections stained by Best's method a considerable number of the cells contains a small linear or crescentic group of minute granules of glycogen in their periphery against part of the cell-membrane. A very few cells contain a larger, denser group of small granules. Larger granules of glycogen lie upon the free surface of cells lining alveolar lumina. No fatty substance is demonstrated by Herxheimer preparations except some crystals in an alveolar space. The nuclei are almost all deeply stained, but show a clear structure ; in the larger examples one or more nucleoli are seen. There is a considerable number of large alveolar spaces which contain a coagulum which is usually slightly, sometimes deeply, oxyphil. The cells which bound them are chiefly of the smaller more deeply stained kinds. Tissue-mast-cells are scattered through the interacinar septa.

FIG. 196.—*Case* 4. Generalized osteitis fibrosa. Larger right parathyroid tumour and smaller right parathyroid tumour removed at second operation. (*Actual size.*)

2. *Smaller Right Parathyroid Body.*—The gland is divided into four large and several small lobes by septa of areolar and denser fibrous tissue. The lobes are subdivided by delicate vascular septa into acini, the size and shape of which depend essentially upon whether they contain principal cells or oxyphil cells. The principal cells occupy small rounded acini. They are usually grouped in a solid mass with cubical cells in the periphery, but frequently in one or more layers round a lumen containing oxyphil coagulum. The latter is usually thin and scanty. Some solid acini consist of a single ring of short columnar cells. Scattered oxyphil cells are found amongst the principal cells in these small acini ; oxyphil cells also fill acini of similar size and shape, occasionally surrounding a lumen. Most of the oxyphil cells, however, occupy large nodular areas in which Laidlaw's stain shows the acini to be considerably larger and of less regular shape. These areas correspond to the purplish areas seen with the naked eye. The largest lobe differs from the others in being rounded, and it is occupied almost completely by oxyphil acini. It is impossible to measure the principal cells accurately because there is no visible

membrane between adjacent cells except in the case of a very few dropsical examples. The latter measure 9 μ in mean diameter. The others have a spongy basophil cytoplasm and appear to be from 8 to 9 μ. All have nuclei of 5 μ. Many of the principal cells contain numerous isotropic spheres, up to 3 μ in diameter, that are stained pale yellow in Herxheimer preparations. Where the cells surround lumina the spheres lie in the cytoplasm of the free ends of the cells. With the exception of a very few deeply oxyphil examples the oxyphil cells have a basophil membrane and resemble those in the large gland. Those that lie isolated amongst the principal cells are usually, however, smaller, measuring 8 to 9 μ with nuclei of 5 μ. The oxyphil cytoplasm is frequently found in large globules, some as large as red corpuscles, or forms a net of lumps of various sizes enclosing irregular vesicular spaces. These appearances are probably artificial, because frozen sections had been taken from the tissue before it was embedded, and in order to obtain them as quickly as possible the formaldehyde had been heated. The nuclei in the larger oxyphil cells are of the same sizes as in the previous section, a few giant examples reaching 9 μ. The nuclei of both the principal and oxyphil cells are stained deeply, but show a definite structure. No preparations of this gland were made to demonstrate glycogen. The oxyphil cells occupy more than half the area of the gland.

Remarks.—The larger gland is occupied completely by oxyphil cells, which almost all have the structure of pale oxyphil cells although most approach the dark type in depth of eosinophilia. Many contain a little glycogen. In the smaller gland the appearances indicate that lobes are being successively converted into tumour-like masses by the replacement of principal cells in small acini by similar oxyphil cells and by the subsequent multiplication of the oxyphil cells. These appearances are strongly in favour of a functional hyperplasia as opposed to an autonomous neoplasm. The hyperplasia in this case resembles that in *Case* 3 in that it consists of oxyphil cells, and almost entirely of pale oxyphil cells. It differs in that there is very much less dropsical separation of the oxyphil granules and less glycogen in the cells.—H. M. T.

Subsequent Progress.—Before leaving the operating theatre one litre of 10 per cent glucose containing 50 units of insulin was given intravenously. On recovery from the anæsthetic the patient's voice was hoarse, and laryngoscopy revealed complete paralysis of the right vocal cord. In view of the fact that two parathyroid tumours had been removed, intramuscular injections of calcium gluconate were commenced the day after operation, 10 c.c. of a 10 per cent solution being given three times a day (*Fig.* 192). The high calcium diet was supplemented by large doses of calcium lactate, up to 15 grm. a day. A 5 per cent solution of calcium chloride was kept in readiness for intravenous use but was never required. The level of the serum calcium rapidly dropped until four days after operation it was 8·9 mgrm. per 100 c.c. The patient was restless and irritable, but there was no objective sign of tetany. At this point parathormone was given by intramuscular injection in increasing doses up to 30 units three times a day. Twelve days after operation the Chvostek sign was positive for the first time, the level of the serum calcium being 7·8 mgrm. per 100 c.c. There were no tinglings nor cramps, and the Trousseau sign was never positive. The Chvostek sign was negative on the fourteenth day after operation, and from that time no manifestation of tetany occurred. Two weeks after operation treatment by ultra-violet irradiation was commenced and carried out for four weeks. Five weeks after operation calcium gluconate injections were discontinued and a week later parathormone was given for the last time. Three weeks after operation the patient was able to walk with the aid of a stick, and four weeks later she left hospital, walking up and down stairs unaided. She pointed out that the readiness to become nauseated and to vomit had gone.

Shortly afterwards she was severely ill with bronchopneumonia, and this was followed by an abscess in the left iliac fossa from which 250 c.c. of pus were evacuated. Five months after removal of the parathyroid tumours she was again well and able to walk alone. The voice was almost normal.

Calcium and Phosphorus Metabolism after Operation.—As already stated, removal of the thyroid adenoma did not abolish the hypercalcæmia, whereas after removal of the parathyroid tumours the serum calcium fell abruptly. It reached its lowest point, namely 7·4 mgrm. per 100 c.c., on the eleventh day after operation (*Fig.* 192). By this time the plasma phosphorus level had risen to 2·5 mgrm. per 100 c.c. Subsequently the serum calcium gradually rose, until 7 weeks after operation it was 9·4 mgrm. per 100 c.c., although all treatment except a high calcium diet had ceased. Plasma phosphatase 0·635 mgrm. Six weeks after operation the calcium output in urine and fæces was estimated for one three-day period on the same low calcium diet as before. The figures both for urine and for fæces were as low as those found in cases of post-operative tetany (*Fig.* 180).

Remarks.—It is worthy of note that a parathyroid tumour measuring 7·5 cm. in its greatest dimension can be so deeply situated in the neck as to defy palpation. There are certain cases recorded in the literature (Barrenscheen and Gold, 1928; Bauer, Albright, and Aub, 1930; Wendel, 1930, *Case* 2) where the evidence of hyperparathyroidism is conclusive and yet no parathyroid tumour was discovered at operation. In recording his case Ball (1930) discusses the possibility that the tumour was missed at operation. In all these cases it would seem imperative to explore the neck again. Removal at operation of two parathyroid tumours has been recorded previously (Beck, 1928). In this case post-operative tetany occurred on the fifth day, accompanied by a psychosis. The patient died of exhaustion on the twentieth day. In such circumstances intravenous calcium chloride must be used. The size of the tumour evidently bears no relation to the severity of the bone lesions, for in *Case* 2 the patient was much more severely crippled than in *Case* 4 and yet the tumour measured only 2·3 × 1·5 × 0·9 cm. and weighed only 1·3 grm.

Epigastric pain, anorexia, and nausea have been described in hyperparathyroidism (Ball, 1930). The rapid disappearance of vomiting after removal of a parathyroid tumour has also been recorded (Pemberton and Geddie, 1930; Rosenbach and Disqué, 1930).

CLINICAL CHARACTERISTICS OF HYPERPARATHYROIDISM.

In the following description are included the cases from the literature summarized above and also the four cases described at length in this article. It will be seen that the symptomatology of hyperparathyroidism does not rest with the skeleton alone.

Satisfactory proof of hyperparathyroidism now exists in 32 cases of generalized osteitis fibrosa. In 21 of these a parathyroid tumour was removed by operation, in 2 cases two parathyroid tumours were removed, and in 4 cases no parathyroid tumour was found at operation. The remaining 5 cases were not operated upon, but proof was obtained by autopsy of a parathyroid tumour in 3 cases, and of two parathyroid tumours in 1 case. The condition is reported twice as frequently in women as in men, the commonest ages being 30 and 55. Pain and tenderness in the bones were common, and

osteoclastomata occurred in more than half the cases. Spontaneous fractures were recorded in 14 cases. Thirst and polyuria occurred in 5 cases, renal calculi in 10 cases, and hæmaturia in 1 case. Occasionally renal colic was the presenting symptom. Hypotonicity of muscles was described in 7 cases. In only 6 cases was the parathyroid tumour palpable in the neck. The largest tumour removed measured 7·5 × 5·0 × 1·8 cm. and weighed 26·2 grm., and yet it had not been palpable in the neck owing to its situation behind the trachea. The size of the tumour bears no relation to the severity of the bone lesions, for in the most severely crippled patient the tumour measured 2·3 × 1·5 × 0·9 cm. and weighed only 1·3 grm. Nausea and vomiting, sometimes with abdominal cramps, have been described. Wasting is common in advanced cases. In those cases where radiograms are mentioned there was greatly diminished density of bone shadows. This is best demonstrated by the controlled method. Sometimes there was radiological evidence of cysts, but these only rarely expanded the corticalis. The serum calcium figures varied between 12·6 and 23·6 mgrm. per 100 c.c., the plasma phosphorus between 1·0 and 2·7 mgrm. Where the plasma phosphatase was estimated it was invariably high. The output of calcium in the urine varied from a slight increase to eight times the normal figure.

In the majority of cases pain in the bones was abolished immediately after operation, and the mechanism of this is difficult to conceive. Decrease in size of osteoclastomata within a few weeks after operation has been twice recorded. Restoration to normal of the menstrual function has also been observed. In three cases removal of the tumour promptly abolished polydipsia and polyuria. In one case renal calculi began to break up a few weeks after operation and were passed into the bladder. In many cases the levels of the serum calcium and plasma phosphorus and the excretion of calcium in the urine were restored to normal. Sometimes there was temporary hypocalcæmia and even oliguria, with subnormal excretion of calcium in the urine. In all five cases where it was recorded after operation the plasma phosphatase remained high; in one of these it showed no alteration even seventeen months later. Latent tetany after operation was common, and manifest tetany often occurred, with marked variations in severity. It was fatal in one case only, where two parathyroid tumours were removed. Nevertheless removal of two parathyroid tumours is not necessarily fatal, nor even necessarily accompanied by post-operative tetany. In one case tremor and acute mania occurred three weeks after operation, at a time when the serum calcium had dropped to 6·6 mgrm. per 100 c.c. The condition was completely relieved in three days by the use of parathormone injections in conjunction with a preparation of calcium given intravenously. This latter procedure must undoubtedly be regarded as the essential treatment of severe post-operative tetany following removal of a parathyroid tumour. The post-operative treatment should include a high calcium diet and ultra-violet irradiation as routine procedures.

Symptomatic improvement almost always occurs after removal of a tumour. Not only is pain in the bones abolished, but there is marked gain in weight, and many crippled patients have been able to dispense with sticks and crutches. In one case, however, pain in the bones was not entirely

abolished eighteen months after operation. Where no parathyroid tumour was discovered removal of a normal parathyroid gland had no good effect in two cases, but removal of two normal parathyroid glands led to considerable symptomatic improvement in another. Some authors claim that an increase in density in the radiographic shadows of bones was to be seen in their cases a few months after operation. It is of great interest that three and a half years after operation Mandl could demonstrate no such change in his case. Should there be special reasons contra-indicating operation upon the neck, or sh uld no tumour be found, the patient may be treated with irradiated ergosterol in the hope of increasing the apposition of bone. In at least one case good evidence has been obtained of the effect of such treatment in increasing the density of bone as judged by radiograms.

OPERATIVE TECHNIQUE.

Mr. A. J. Walton has kindly made the following note on the technique he employs at operation.

A wide exposure is essential, for not only is it necessary to explore all the parathyroid glands, but also, as our limited experience has already shown, it is sometimes necessary to search behind the trachea and in the mediastinum. In all our cases a wide collar incision has been made, the sternomastoids freed and widely retracted, and the pretracheal muscles between them divided transversely in one sheet at the level of the centre of the isthmus of the thyroid gland. The flaps thus formed are dissected up as high as the upper poles of the lateral lobes and as low as the sternum. This gives a much wider exposure than a vertical split of the muscles, and if they are carefully sutured afterwards no deformity or weakness results.

The lateral lobes of the thyroid gland are now rolled inwards in turn to expose the sites of the normal parathyroid glands. These are examined in turn, and a tumour may at once be found in the normal site or a little lower. In a case published elsewhere (Hunter, 1929; 1930, *Case* 4) a tumour measuring 3·7 × 3 cm. was at once found at the site of or a little lower than the left inferior gland. If no tumour be observed in the usual site, a finger should be passed into the thorax on either side of the trachea, for the tumour may pass down in this situation. In *Case* 3 a tumour 6·8 × 2·8 cm. was easily detected in the upper part of the thorax on the left side of the trachea and was readily drawn up into the neck. In certain cases no tumour is visible. A difficulty may arise if there be a small thyroid adenoma, for a parathyroid tumour may be situated in the substance of the thyroid gland. In *Case* 4 this error was made in spite of the fact that Professor Turnbull, who was present, was of the opinion that the tumour was a colloidal adenoma of the thyroid gland. This error should be guarded against, because the yellowish-brown appearance of a parathyroid tumour usually makes it distinctive even to the naked eye. In our case the error was only made clear after histological examination, and a second operation revealed a parathyroid tumour behind the trachea. In *Case* 2 also the tumour lay behind the trachea. This anatomical relationship probably explains many of the reported cases where the tumour has not been found. If, therefore, a tumour is not recognized in

one of the ordinary positions nor in the thorax at the side of the trachea, the right thyroid lobe should be rolled over to the left and the carotid sheath retracted outwards until the right inferior thyroid artery is visible as a band passing to the right lobe. A small incision is then made into the fascia above it and just *behind* the œsophagus. The prevertebral space is thus entered and a small tumour may be immediately revealed as in *Case* 2. If it is not, a finger can be inserted into the space and passed down behind the œsophagus into the thorax. At the second operation on *Case* 4 this was done and a soft fleshy mass measuring 7·5 × 5 cm. was easily felt lying on the first and second thoracic vertebræ. With a few movements of the finger it was freed from its adhesions and pulled up into the neck, when it was found to have a narrow vascular pedicle attached to the inferior thyroid artery. This was divided and the tumour removed. In the case of a tumour arising on the left side it would be necessary to make an incision through the fascia on the left side. The tumour could then be everted and the pedicle ligatured. The cavity after removal appears to be of remarkable depth, but in our case the elevation of the tumour was accomplished with extraordinary ease. A tube is inserted into the cavity, the pretracheal muscles sutured with catgut, and the skin incision closed. We have usually left the tube in for two or three days.

PATHOGENESIS OF GENERALIZED OSTEITIS FIBROSA.

(Professor H. M. Turnbull.)

Generalized osteitis fibrosa is characterized by changes in the skeleton, enlargement of one or more parathyroid glands, hypercalcæmia, and an increased excretion of calcium in the urine.

The changes in the skeleton are lacunar resorption, apposition, fibrosis of the marrow, and the formation of osteoclastomata and cysts. Lacunar resorption is the predominant change. Radiography, and histological examination of the skeleton at necropsy show that resorption has led to a general osteoporosis, which, however, varies in degree in different places. But formation of bone does not cease. Bone is seen in process of formation in almost all sections taken from the more severely affected parts of the skeleton, and previous formation of bone is shown by an extensive, and in places complete, replacement of lamellar bone by trabeculæ of woven bone. Apposition is, indeed, frequently the predominant active process in a segment examined. The combination of resorption and apposition is shown by osteoclastic and osteoblastic activity upon different trabeculæ in many sections, and even upon the same trabecula in some sections. The interplay of the two processes is further witnessed by trabeculæ that are composed of several separate systems of woven bone. In focal areas the new spongy bone that has been formed may actually exceed in bulk the normal spongiosa and compacta, for instance in some of the expansions of the ribs in a case previously reported (Hunter, 1930, *Case* 3) and in the massive calvaria of *Case* 1.

Where apposition is taking place the depth of the osteoid zones varies in different places in the same case, and the maximal depth varies in different cases. The essential abnormality in rickets and osteomalacia is cessation of

calcification, and the characteristic histological abnormality that results is an excessive amount of osteoid tissue. Consequently, the disputed question of whether or not there is a true osteomalacia in generalized osteitis fibrosa depends upon whether the amount of osteoid tissue is, or is not, excessive. Pommer (1885) showed that all bone when first formed is osteoid and becomes calcified later. Osteoid zones are, therefore, present upon all trabeculæ during osteoblastic activity. The depth of the zones varies with the rapidity of formation. Thus, the depth is greater in the rapidly growing bones of children than in the bones of adults, and is greater still in the healing of fractures. In order to determine whether there is an abnormal delay in calcification it is necessary first to determine whether the osteoid zones are associated with osteoblastic activity and to form some estimation of that activity, and secondly to compare their depth with zones measured in healthy subjects. Some estimation of the activity is obtained from the form and number of the osteoblasts. The osteoblasts are cells of the fibrous reticulum of the marrow in a stage of functional activity. The resting cells in the fibrous marrow are spindle cells with very scanty cytoplasm. The active osteoblasts upon the osteoid zone are plumper and have a much more abundant, finely granular, more oxyphil cytoplasm. In very rapidly growing bones one or two rows of cells that show transitional characters are sometimes seen between the row of osteoblasts upon the osteoid zone and the resting cells of the marrow. Further, the active osteoblasts are more numerous, being at a shorter distance from one another, than the resting cells. When apposition ceases the osteoblasts return to the form and number of resting cells. The importance of forming an estimation of activity is illustrated by the example in this paper of a condition other than osteitis fibrosa (*Case* 9). Many of the osteoid zones were deeper than in healthy adults and children, but the depth seldom exceeded that in healing fractures, and the amount of osteoid tissue was very slight (*see Fig.* 195) compared with that in typical cases of osteomalacia. The osteoblasts, however, appeared to be in a state of rest or of very slight activity. The unusual depth could not, therefore, be attributed to exceptional activity of apposition, but indicated delay in calcification. Disturbance of calcification was further indicated by partial calcification within some zones. The histological diagnosis of osteomalacia was confirmed by the effects of appropriate treatment. In measuring the depth of osteoid zones it is necessary to select zones that have been cut strictly at right angles to their surface. In such sections the osteoblasts are at their narrowest and of spindle shape. When the cells are seen in full-face the nuclei are rounded, the cytoplasm is much more abundant, and the outline polygonal. In oblique sections the appearances approximate to those of cells seen in full-face. In a skeleton fully examined (Hunter, 1930, *Case* 3) and in *Case* 1 and *Case* 4 of this paper it is possible to examine portions of bone that are free from fibrosis. In *Case* 3, 1930, and *Case* 1 such trabeculæ are almost everywhere free from osteoblastic activity, and are fully calcified; where there is any osteoblastic activity it is relatively slight and the osteoid zones are very narrow. In *Case* 4 there are many osteoid zones upon trabeculæ that are not involved in fibrosis; the depth is within the limits of those in healthy children, and osteoblastic activity is as great as in children. When the trabeculæ within

the fibrous marrow are considered, in *Cases* 1 and 4 the zones are never deeper than in the bones of young children, in the skeleton fully examined they are seldom deeper, in *Cases* 2 and 3 and *Case* 4 of a previous paper (Hunter, 1930) they are usually deeper. In the four cases, however, in which the maximal depth exceeds that in young children, it is within the limits measured in healing fractures in healthy adults, and osteoblastic activity is as great as in healing fractures. Examination of these six cases, therefore, of generalized osteitis fibrosa associated with parathyroid enlargement shows that in the fibrotic areas apposition is frequently as rapid as in the healing of fractures and the osteoid zones are correspondingly deep, but neither here nor in the available parts of the skeleton that are free from fibrosis is there evidence of the delay in calcification which characterizes osteomalacia and rickets.

Schmorl (1926) said that the question of the presence of osteomalacia in generalized osteitis fibrosa cannot be decided by examination of the diseased portions of bone involved in fibrosis, because there is always active apposition there and abundant osteoid tissue is consequently to be expected. He examined, therefore, the 'healthy' parts of the bone in 44 cases. In 8 he found evidence of osteomalacia, in that osteoid zones were present, which certainly were shallower than those in his very numerous examples of osteomalacia but yet were found everywhere. The comparative shallowness he attributed to the presence of a very considerable atrophy in the bones. He made no mention of the condition of osteoblastic activity upon these zones. In the remaining 36 cases there were no calcium-free zones in the parts free from fibrosis. He said, therefore, that Lang (1926), who considered that generalized osteitis fibrosa is always combined with osteomalacia or late rickets, and Stenholm (1924), who came to an exactly opposite conclusion, were both wrong. He concluded, however, that generalized osteitis fibrosa is an independent, peculiar disease of the skeleton which has no relation to *florid* rickets or *florid* osteomalacia. Schmorl evidently in this paper made no distinction between the multiple focal areas of osteitis fibrosa and the generalized osteitis fibrosa which Hunter (1930) has differentiated by both radiographic examination and estimation of calcium metabolism. In the discussion following the review of osteitis fibrosa by Christeller (1926) in the same year, Schmorl said that he had examined the parathyroid glands in all his cases of osteitis fibrosa and had found enlargement in only four cases. In these four cases there was a combination with osteomalacia. Apparently, therefore, Schmorl found the above evidence of osteomalacia in all his four cases of generalized osteitis fibrosa associated with parathyroid enlargement, and in four out of forty cases of osteitis fibrosa without parathyroid enlargement. Schmorl (1926) described the frequency of rickets and osteomalacia in Dresden as enormous. Osteomalacia might well, therefore, be an accidental complication of generalized osteitis fibrosa in his material.

Fibrosis of the marrow is a conspicuous feature. It is very widespread, but is not universal. As in *Case* 4 there may be great osteoporosis whilst fibrosis is focal and slight. In an extensive examination of a whole skeleton, however, there was no section in which fibrosis was completely absent. Where it is most sparse it is confined to bays eroded upon the surfaces of the compacta or trabeculæ in the spongiosa, and to Haversian spaces eroded within the compacta or within the trabeculæ of the spongiosa. In greater amount it forms a zone upon one surface of greatly eroded trabeculæ in the spongiosa or forms a sheath all round such trabeculæ. In still greater amount it forms broad bands in the spongiosa that enclose groups of small or slender trabeculæ. All these grades are frequently seen in a single section, as is

shown in the head of the humerus in *Case* 1 and very conspicuously in the bodies of the vertebræ in a case previously reported (Hunter, 1930, *Case* 3). In part of the bodies of these vertebræ trabeculæ of lamellar bone form a spongiosa of normal mesh and show only focal areas of fibrosis that fill bays eroded upon their outer surfaces or fill Haversian spaces eroded within them; other trabeculæ of lamellar bone are centrally split to a greater or less extent by eroded spaces filled with fibrosis; others are split into smaller pieces which are completely embedded in fibrosis; finally, areas are occupied by a close network of broad bands of fibrosis containing very closely packed small trabeculæ of newly formed, woven bone. In its greatest amount the fibrosis forms in portions of the long bones that normally have a medullary cavity free from bony trabeculæ a fibrous compacta containing small bony trabeculæ, and in spongy bones or spongy portions of bones fully occupies both the compacta and spongiosa. In the former case the intimate relation of the fibrosis to the bony skeleton is most striking (*Case* 1, *Fig.* 176). In the latter case there may be focal expansions, particularly of the ribs. Where the fibrosis forms broad bands in the spongiosa or extends through the corticalis, the included trabeculæ are sometimes (*Case* 3) remnants of old bone, but usually they consist of woven bone formed during the disease. Where the fibrosis extends throughout both corticalis and spongiosa—for instance, in expansions—trabeculæ of woven bone may extend throughout, forming an osteosclerotic nodule; but usually they are confined to the periphery, leaving in the centre a fibrous area of variable size. The smaller focal areas of fibrosis are almost invariably associated with very active lacunar resorption, shown by numerous large osteoclasts, but sometimes with an active apposition. More extensive fibrosis is associated with exceptional activity of either resorption or apposition, or with evidence of very great previous resorption. On the other hand, where fibrosis is absent osteoporosis may be great and bear witness to much previous resorption, but the osteogenetic marrow is almost invariably at rest; occasionally it shows a slight osteoblastic activity.

Study of the fibrosis of the marrow thus shows first that it is intimately associated in position with bone, appearing first upon its surface and later ensheathing or largely replacing it, secondly that it is closely associated with exceptional activity of resorption or apposition. In infections the osteogenetic fibrous tissue of the marrow reacts like other soft tissues, and when the resulting granulation tissue is little differentiated and cellular it tends to cause resorption of bone, and when it is more differentiated and fibrous it tends to form bone. The fibrosis of the marrow and the resorption and apposition of bone in generalized osteitis fibrosa might, therefore, be the result of a spreading inflammation of the marrow. In that case the intimate association of the fibrosis with bone could only be explained by the excitant of the inflammation being present within bone. There is no histological evidence of this: the fibrosis appears initially upon the surface of portions of bone that appear to be perfectly normal in structure. Cellular proliferation of the osteogenetic marrow is excited, however, not only by inflammatory stimuli but by the stimuli that govern normal apposition and resorption of bone. In resorption and in apposition, even of lamellar bone, there appears always to be some proliferation of the cells of the osteogenetic, as opposed

to the hæmatogenous, marrow. In the more actively growing portions of the bones of the newly born a proliferation of spindle cells immediately behind the ripe osteoblasts upon the trabeculæ sometimes gives the appearance of a zone of slight fibrosis upon the trabeculæ. In severe rickets and osteomalacia focal areas of fibrosis may lie upon trabeculæ, zones of fibrosis may ensheath trabeculæ, or there may be a more extensive fibrosis. The fibrosis resembles that in generalized osteitis fibrosa, and has the same intimate connection with bone. In severe rickets the weakening of the bone following arrest of calcification leads in places to the formation of osteoid tissue in excess of the amount of bone in a normal skeleton, as is shown by the excessive width of the osteoid trabeculæ and by the buttressing of bowed corticalis. Osteoblasts are numerous and large upon the osteoid zones. There can be little doubt that the osteogenetic marrow is excited here to exceptional activity by stimuli of strain and stress. The associated zones of fibrosis are doubtless caused by the same stimuli, and are probably merely expressions of marrow in a condition of exceptional osteogenetic activity. If such fibrosis of the marrow is merely a sign of exceptional activity, and if it can be shown that the enlarged parathyroid glands in generalized osteitis fibrosa are stimulating an excessive lacunar resorption of bone, then the fibrosis in this disease can be attributed primarily to excessive stimulation of resorption by parathyroid secretion and secondarily to excessive stimulation of apposition by strain and stress upon bone weakened by great resorption.

The engorgement that is usually present in the fibrous marrow can be attributed to functional activity of the osteogenetic marrow. Thus, engorgement is associated with activity of the hæmatogenous marrow, as is shown conspicuously in the small focal areas in adipose marrow which mark the beginning of an extension of blood-formation. Red marrow, indeed, owes its colour to this engorgement.

Cysts are usually numerous. They were very numerous in one case previously reported (Hunter, 1930, *Case* 3), and the following remarks upon their formation are based chiefly upon a study of this skeleton. Many, particularly the larger, have a wall of dense, often hyaline, collagenous fibrous tissue. In the others the wall does not differ from the surrounding fibrous marrow. The dense wall appears to be a secondary change, and the cysts that have no specialized wall appear to represent earlier stages in formation. Most of the latter contain a thin albuminous coagulum with or without red corpuscles, others contain a similar coagulum with fat-granule-cells and, rarely, cholesterin crystals; others contain blood or a little fibrinous clot containing red corpuscles; others are empty. Some have a sharply defined, even margin and are lined with a layer of flattened cells that resembles endothelium. In others the margin is not sharply defined, and is obviously formed by the cells of the surrounding tissue, sometimes including osteoclasts. Occasionally the boundary consists of fibrous marrow split into a loose reticulum by hæmorrhage. The cysts most frequently occur in the larger areas of fibrous marrow that are free from bone, but they are not confined to these. Thus, the cyst in the calvaria of *Case* 1 lies in a close net of bony trabeculæ. In the centres of these larger areas of fibrosis vessels are scanty or absent, and there is usually degeneration. The commonest

degeneration is a fibrinoid degeneration preceded by extravasation of red corpuscles, but there may be severe hæmorrhage, or multiple focal areas of serous œdema, or, rarely, a severer degeneration and necrosis associated with the accumulation of fat-granule-cells and cholesterin crystals. Organization of thrombosed vessels is also seen. In the periphery of the larger areas of fibrosis there are often dilated vascular spaces, of which some are distended with blood but many are empty or contain a few red corpuscles or a little thin albuminous coagulum. Such dilated vascular spaces are often present in the immediate neighbourhood of cysts. The cysts that have a sharply defined margin lined with a layer of flattened cells resemble these dilated spaces so closely that an origin from them is strongly suggested. Laidlaw's silver impregnation shows, however, that the vascular spaces have a sharply defined wall, which consists at least of a thin sheet of delicate fibrils; and the early cysts rarely have a definite and continuous limiting membrane. It is rare, too, for the cysts without densely fibrotic walls to have a lining that resembles endothelium, although large cysts with dense walls frequently do. Further, transitions can be followed from irregular areas of focal serous œdema in which the cells of the fibrous marrow are slightly separated by thin coagulum, through rounded areas in which spindle fibroblasts form an ever scantier net in such coagulum, to perfectly spherical cysts that contain coagulum alone. Again, in the neighbourhood of cysts transitions can sometimes be followed from groups of fat-granule-cells to irregular or rounded cystic spaces more or less filled with a granular débris containing fat-granule-cells and cholesterin crystals. If the cysts have a single origin, then the evidence appears to be stronger for origin in œdema and degenerations of the fibrous marrow than in dilatation of vascular spaces. It is possible, however, that cysts arise in both ways. In either case there can be little doubt that the cysts are due to disturbances in the circulation consequent upon the fibrosis of the marrow or the weakening of the bone. It is probable that cysts are also occasionally the result of autolysis of osteoclastomata. Large, ill-defined, cystic spaces, filled with thin coagulum, certainly do occur within osteoclastomata.

The osteoclastomata are areas occupied by numerous large osteoclasts among fibrocytes that are less differentiated than in the remainder of the fibrous marrow. In number and size the osteoclastomata vary greatly in different cases. Some are minute (*Fig.* 187); others form large masses that expand part (*Cases* 2 and 3), or the whole, of the circumference of large long bones. It has been pointed out (*Case* 2) that it is impossible to attribute such tumours to collections of osteoclasts that have persisted *in situ* after eroding bone. Areas of fibrinoid degeneration are preceded by extravasation of red corpuscles, and osteoclasts are usually numerous in such areas. Further, osteoclastomata are frequently associated with hæmorrhage and the accumulation of iron-pigment. Again, some of the osteoclasts occasionally contain red corpuscles or hæmosiderin. But hæmorrhage may be trivial or absent within osteoclastomata, and the number of osteoclasts that do contain corpuscles or pigment is relatively minute. It is impossible, therefore, to regard the osteoclastomata as areas in which osteoclasts have been stimulated to multiply as scavengers of hæmorrhage. Osteoclastomata have been

observed to disappear after excision of enlarged parathyroid glands (Barr, Bulger, and Dixon, 1929; Hunter, 1931). Their disappearance after excision of enlarged parathyroid glands suggests that they are areas of osteogenetic marrow that have been stimulated by excessive parathyroid secretion to an exaggerated osteoclastic activity. It has been argued that the fibrosis of the marrow represents osteogenetic marrow in an exceptional state of activity, and that this activity might be the result of excessive parathyroid secretion. In their origin the osteoclastomata would thus be akin to the fibrosis of the marrow, and the less differentiated form of the fibroblasts within them is in keeping with a more exaggerated activity than in the rest of the fibrous marrow.

According to the above interpretation of the histological changes in generalized osteitis fibrosa in man all the abnormalities in the bone could be attributed primarily to parathyroid secretion causing an excessive stimulation of osteoclastic resorption. Clinical observations bring evidence that the enlarged parathyroid glands deprive the skeleton of calcium. The hypercalcæmia that characterizes the disease disappears almost immediately after the removal of the enlarged glands, and the skeleton becomes stronger. Further, the administration to man of parathormone brings into the blood not only calcium, but lead (Hunter and Aub, 1926), radium (Flinn and Seidlin, 1929), and other elements that are known to be stored in the bones in close association with calcium. To prove that the bone of the skeleton is reduced in this process, and is reduced by osteoclastic resorption, requires animal experiment. Bauer, Aub, and Albright (1929) found naked-eye evidence of loss of trabeculæ in the spongiosa of the long bones of rabbits which had been injected with increasing doses of parathormone. They made no microscopic examination, however, so that if their experiments proved that parathormone reduces the skeleton, the method of reduction was not determined. In order to supply this important deficiency Dr. F. B. Byrom in May, 1930, made a small series of similar experiments under Dr. Hunter's direction. After handing the bones to me Dr. Byrom went to America. It was intended to allow the bones to decalcify in Müller's solution until his return, but when this article was being written as many of the bones were embedded and cut as time permitted.

Dr. Byrom chose a litter of seven rabbits, two months old. All the rabbits received an unrestricted diet of bran, oats, lettuce, and cabbage. Four rabbits (316, 317, 318, 319) were given daily subcutaneous injections of parathormone (Collip) in increasing doses, beginning with 1 unit and rising to a maximum of 50 units in one animal (316). The three others (313, 314, 315) were kept as controls on the other side of the animal house. All rabbits were marked by a stamped metal ribbon clipped round a leg. No symptoms of hypercalcæmia were observed. The injections were begun on May 6. *Rabbit* 317 was killed on June 16, having received in the 41 days 374 units in all; control rabbit 314 was killed at the same time. The serum calcium of rabbit 317 was 12·9 mgrm. per 100 c.c. on May 6 before the first injection, 9·1 on June 4, and 7·7 on June 10. The plasma phosphatase of the control was 0·315 on June 4. *Rabbit* 318 was killed on July 23, having received in the 78 days 610 units; control rabbit 313 was killed at the same time. The serum calcium was 13·4 on May 6, 11·6 on May 16, and 10·8 on June 24; the plasma phosphorus was 7·0 mgrm. on June 24. In the control on June 24 the serum calcium was 9·2 and the plasma phosphorus 7·5; on June 4 the plasma phosphatase

was 0·369. Rabbits 319 and 316 were both killed on Aug. 15 with control rabbit 315. *Rabbit* 319 had received 770 units in the 101 days. The serum calcium was 13·8 on May 6 before the first injection, 12·0 on May 12, 10·3 on June 24, 9·8 on July 17, and 11·3 on Aug. 13; the plasma phosphorus was 7·5 on June 24; the plasma phosphatase was 0·192 on July 17, and 0·172 on Aug. 13. *Rabbit* 316 had received 2150 units in the 101 days. The serum calcium was 14·5 on May 6 before the first injection, 13·1 on May 12, 12·5 on May 26, 8·4 on June 24, 9·7 on July 17, and 9·5 on Aug. 13; the plasma phosphorus was 5·8 on June 24; the plasma phosphatase was 0·199 on July 17, and 0·147 on Aug. 13. In the control rabbit the serum calcium was 9·0 on June 24, and 9·7 on Aug. 13; the plasma phosphorus was 6·0 on June 24; the plasma phosphatase was 0·294 on May 26, and 0·286 on Aug. 13.

When the rabbits had been killed the long bones were dissected out, and each bone from the injected animal was radiographed beside the corresponding bone of the control. The bones of both animals were then divided longitudinally; one half was digested in pancreatic solution, the other was reserved for histological examination. When the bones were examined with the naked eye the zone of proliferating cartilage in rabbit 317 was seen to be narrower and less translucent than in the control, whilst the zone of spongiosa beneath was narrower. In rabbit 318 the zone of proliferating cartilage did not differ from that in the control; but the depth of the spongiosa beneath was strikingly less, as is well shown in photographs of the macerated bones. It appeared, therefore, that in spite of the fall in the serum calcium the experiments showed in the injected rabbits a depletion of the reserve of calcium in the bones such as had been observed by Bauer, Aub, and Albright.

Microscopic Examination.—In all the bones examined the provisional calcification of cartilage is complete and there is no irregularity in chondral ossification, whilst the zones of osteoid tissue are covered by closely packed, large osteoblasts, and where they are cut at right angles to their surface, their depth shows little variation and lies well within the limits of the zones in young children. There is, therefore, no evidence of rickets or osteomalacia.

Rabbit 317 (374 *Units of Parathormone*) *and Control.*—Two ribs and a piece of of parieto-occipital bone, decalcified in Müller's solution, have been examined in each case. In the ribs in both cases there is no obvious abnormality in the spaces between the trabeculæ of calcified cartilage upon which little or no bone has been deposited; the spaces contain a few osteoclasts and numerous osteoblasts at the sides of the central capillaries. In the scanty spongiosa which forms the rest of the metaphysis there are numerous osteoclasts in Howship's lacunæ, and where these are absent osteoblasts usually lie upon osteoid zones. Osteoclasts frequently lie upon the truncated diaphysial ends of the trabeculæ. The trabeculæ are surrounded by a zone of delicate fibrosis. The corticalis for seven millimetres is reduced to a narrow spongiosa by cavities formed by erosion from the periosteal and endosteal surfaces and by erosion about vascular canals. The cavities are filled with fibrous marrow, and are lined by osteoclasts or by osteoid zones covered by osteoblasts. The inner surface of the corticalis is covered by a zone of fibrosis which unites with the fibrosis in the spongiosa of the metaphysis. Farther away from the epiphysis erosion of the corticalis is less, but is shown by many large Haversian spaces filled with fibrous marrow and lined with osteoclasts, and by deep or long shallow bays eroded from the endosteal surface. The zone of fibrosis upon the inner surface of the corticalis is continued; it varies in depth according to the amount of erosion, and is absent in a few places where there is no evidence of erosion. Active apposition by osteoblasts is present in addition to conspicuous osteoclastic resorption. The marrow within the medulla is bounded above by the fibrosis in the spongiosa and laterally by the zone of fibrosis upon the inner surface of the corticalis. It is an adipose marrow loaded with healthy hæmatogenous cells; it contains no bone and shows no trace of fibrosis. In the occipito-parietal bones the inner and outer tables contain cavities eroded from their surfaces, especially the inner, and cavities eroded round vessels. The tables are frequently interrupted. The trabeculæ in the scanty spongiosa also show erosion. The cavities within the tables are filled with fibrous

marrow, and a zone of fibrosis clothes the inner surfaces of the tables and the trabeculæ wherever they show erosion. Osteoclasts in lacunæ and osteoblasts upon osteoid zones are numerous.

In the ribs of rabbit 317 the trabeculæ of the spongiosa are less numerous than in the control and extend for a shorter distance towards the medullary cavity. Growth in length of the ribs is much less active, as is shown by a shallower zone of cartilage cells in columns, and very much shallower zones of hypertrophied cartilage cells and of calcified chondral trabeculæ with little or no bone upon their surfaces. In the calvaria there is no appreciable difference between the injected rabbit and the control.

Rabbit 318 (610 *Units of Parathormone*) *and Control.*—As macroscopic differences were most obvious in this pair all the bones in process of decalcification in Müller's solution were further decalcified in nitric acid, embedded, and cut. The bones were: portions of two ribs and of the parietal bone; the whole length of the humerus, femur, tibia, and first metatarsal; the tibia included the upper end of the fibula. The bones in both rabbits show changes that are similar to those in rabbit 317 and its control but are of greater degree. In the long bones two or three neighbouring trabeculæ have occasionally been completely removed by osteoclasts in the zone of calcified chondral trabeculæ upon which little or no bone has been deposited. In such spaces there is sometimes a delicate fibrous tissue. Elsewhere in this zone the clefts upon either side of the central capillary contain a few osteoclasts but are otherwise filled with osteoblasts. The spongiosa of the metaphysis is embedded in a dense fibrous tissue and contains a remarkable number of osteoclasts in lacunæ; it also shows, however, many osteoid zones covered by osteoblasts. In a few bones one or two trabeculæ extend from the metaphysis into the medulla. They are clothed partially or completely by a zone of fibrosis. The corticalis for some distance from the epiphysis is greatly reduced and split up by eroded cavities filled with fibrous marrow. In the remainder of the shaft erosion is less, but is shown by conspicuous enlargement of occasional vascular canals within the corticalis and by long shallow cavities upon its inner surface. In general, erosion is greatest near and on the inner surface of the corticalis. Osteoclasts in lacunæ are numerous, but many eroded surfaces are covered by osteoblasts upon osteoid zones. The corticalis is bounded within by a zone of fibrosis, except where erosion is absent. The fibrosis is confined to the spongiosa in the metaphysis, to the surface of trabeculæ that occasionally extend farther into the medulla, and to the inner surface of the corticalis and to the Haversian spaces eroded within the corticalis. The medullary cavity is otherwise normal, except near the centre of the shaft of the femur of rabbit 318. Here a few small trabeculæ of newly-formed bone are embedded in an area of fibrous marrow, and touching the margin of this area is a rounded space which is filled with thin coagulum and has an ill-defined margin. This is the only structure that resembles an early bone-cyst. The bony epiphyses seldom show any abnormality. In some there are a few eroded cavities in the peripheral plate of bone, particularly the part next the junctional cartilage, and a few bays eroded upon trabeculæ of the spongiosa. Fibrosis is confined to such eroded cavities and bays. All the long bones appear to be about equally affected. The parietal bones as in rabbit 317 and its control show erosion associated with fibrosis within and on the surfaces of the inner and outer tables, and on the surfaces of trabeculæ in the spongiosa. The eroded spaces contain osteoclasts or are lined with osteoblasts upon an osteoid zone.

The activity in growth in length of the long bones appears to be the same in rabbit 318 and its control. As was seen in the macerated specimens, however, the spongiosa forms a very much shallower zone in 318 than in the control. The bones of 318 are in general more porotic than in the control, but they show a less intensely active osteoclastic resorption. Although in the control, therefore, osseous tissue is somewhat more abundant, the bones show the appearances of a more acute and greater osteitis fibrosa.

Rabbit 319 (770 *Units Parathormone*), 316 (2150 *Units*), *and Control.*—Time only permitted microscopical examination of two ribs and a longitudinal section of

three vertebræ in each case. The ribs of rabbit 319 show changes that are similar to those in previous animals, but less pronounced. The trabeculæ in the spongiosa are scanty and short. They are ensheathed by zones of fibrosis which are slightly narrower and less dense than in rabbit 317 and its control. The corticalis throughout the length of the section contains many large spaces that are filled with fibrous marrow and lined with osteoclasts in lacunæ. A narrow zone of fibrosis lines most of the inner surface of the corticalis on each side. In rabbit 316 these changes are less marked. The spongiosa appears to be more abundant. There are fewer spaces eroded within the corticalis. The zone of fibrosis upon the inner surface of the corticalis is more focal. In the control rabbit the changes are very similar to those in rabbit 316. There is very little erosion within the corticalis, but there are several large bays, lined by osteoclasts, upon the inner surface. In the bodies of the vertebræ the plates of bone contain a few spaces filled with fibrous marrow and lined with osteoclasts, but otherwise the association of fibrosis with erosion is not seen. In the control rabbit the trabeculæ in the spongiosa are fewer and thinner than in the injected animals. The corticalis is also thinner, and more interrupted; that forming the posterior wall of the bodies is absent in nearly half of its length.

Judged by the ribs, therefore, the skeleton in this group of rabbits shows changes similar to those in all the others. The changes are of slightly less degree than in rabbit 317, which received 374 units of parathormone, and its control, and of much less degree than in rabbit 318, which received 610 units, and its control. Further, within this group the changes in rabbit 319, which received 770 units, are more pronounced than in rabbit 316, which received 2150 units; and rabbit 316 shows no more change than the control rabbit.

The microscopic examination of the bones of the rabbits in Dr. Byrom's experiments has, therefore, given no unequivocal information concerning the action of parathormone on the skeleton, although the changes seen with the naked-eye appeared to confirm the findings of Bauer, Aub, and Albright. The experiments have, however, shown that in the bones of a whole litter of seven, apparently healthy, young rabbits there were changes identical with those that have been given in detail above as characteristic of generalized osteitis fibrosa in man, except that only one doubtful cyst was observed and there were no osteoclastomata. Analysis gives no evidence that the administration of parathormone influenced the condition in any way. The condition varied with age. It was most pronounced in the animals killed when 19 weeks old, and slightly less at the age of 22 weeks than at 14 weeks. Further work can alone determine the prevalence of the condition, and the influence of diet, etc. The parathyroid glands were not examined. The resemblance of the changes in the skeleton to those in generalized osteitis fibrosa in man is so close that the rabbit may possibly prove an animal in which that disease can conveniently be studied. Lévy (1908) described changes in the skeleton of an adult female rabbit which were essentially similar to those described here. The rabbit had had a portion of caseous mesenteric gland from a child inoculated into the anterior chamber of an eye. It died forty-four days later. The skeleton appeared to be normal to the naked eye, but was examined microscopically because calcareous metastases had been found in internal organs and vessels. The parathyroid glands are said to have shown no microscopical change.

Shortly before Dr. Byrom began these experiments Jaffe and Bodansky (1930) and Jaffe, Bodansky, and Blair (1930) had published in America a preliminary report upon similar experiments upon puppies and guinea-pigs.

According to the details published later in the year these authors found that in young guinea-pigs on ordinary diet a single injection of 20 units of parathormone to 100 grm. of body weight produced in the ribs as early as the twelfth hour osteoclastic lacunar resorption of the corticalis and some fibrosis of the marrow at the costochondral junction. At the eighteenth hour the resorption was greater, the enlarged spaces eroded in the corticalis were filled with fibrous marrow, and formation of new bone at the costochondral junctions had ceased. At the forty-eighth hour there was a spontaneous fracture of the greatly thinned corticalis. In young fasting guinea-pigs similar results were obtained, but in adult guinea-pigs, either fed or starved, there were no changes in the bones that could be attributed to the parathormone. By repeated injections of parathormone over long periods into puppies and young guinea-pigs they produced great general osteoclastic resorption, extensive fibrosis of the marrow, small cysts, and metastatic calcification in the subcutis and viscera. The parathyroid glands were atrophied. In these experiments very little osteoid tissue was found, except at the site of fractures. Experiments were, therefore, devised to allow repair, the injections being discontinued periodically and the animals being killed three to seven days after the last injection. During the period of repair extensive subperiosteal callus was formed, a considerable amount of bone was laid down upon the wide Haversian spaces, and a considerable amount of osteoid tissue was formed at the costochondral junction and in the metaphysis. The osteoid tissue depicted in the shaft of a long tubular bone of a guinea-pig in *Fig.* 7 (Jaffe, Bodansky and Blair, 1930) is evidently coarse-fibred.

The authors found necrosis of the cells of the hæmatogenous marrow in all dogs that died from acute hyperparathyroidism. They believed that in acute hyperparathyroidism there was also destruction of other lymphoid tissues. They considered that there could be little doubt that in prolonged treatment with parathormone the fibrosis of the marrow was in part an expression of the healing of injured marrow; they frequently refer to fibrosis of the marrow as scarring of the marrow. But the authors point out as a striking feature the absence of this acute degeneration of the marrow in animals that were protected from acute hyperparathyroidism by the administration of preliminary small doses of parathormone. Further, fibrous marrow appeared at an early stage within the Haversian spaces that were being eroded in the compacta. In such spaces there is no hæmatogenous marrow which by destruction could stimulate fibrosis. Moreover, from their descriptions and illustrations the fibrosis appears to have had exactly the same distribution and intimate relation to bone as in Dr. Byrom's rabbits and in generalized osteitis fibrosa in man. They considered the cysts to be vascular spaces dilated secondarily to disturbances of the circulation.

Jaffe, Bodansky, and Blair, therefore, claim to have caused typical generalized osteitis fibrosa with cysts in young guinea-pigs and dogs by the prolonged administration of parathormone. They thus appear to have proved conclusively the correctness of the interpretation of the changes in the skeleton in man that has been suggested above from examination of the histological processes. Their experiments were very numerous, and evidently performed with great care; in those upon guinea-pigs the bones from nineteen untreated young and old, fed and fasting, animals were studied as controls. Further, the animals were puppies and young guinea-pigs, and not young rabbits. It appears, therefore, unjustifiable to doubt their results, but for anyone who has recently had such a surprising experience as the examination of Dr. Byrom's material unquestioning belief is impossible until the experiments have been confirmed by others. The condition in Dr. Byrom's treated and untreated rabbits appears to have been identical with the condition described by these authors in their guinea-pigs, except that they found little osteoblastic activity when the injections were not interrupted.

It remains to find an explanation of the enlargement of the parathyroid glands. Adding two cases previously published (Hunter, 1930, *Cases* 3 and 4) we have examined six cases. In two cases (*Cases* 1 and 4 of this paper) two glands were enlarged. The measurements were: *Case* 3, 1930, 2 × 2 × 2 cm.; *Case* 4, 1930, 3·7 × 3 × 3 cm.; *Case* 1, 2·8 × 2·5 × 1·8 cm. and 1·1 × 1·1 × 1·1 cm.; *Case* 2, 2·3 × 1·5 × 0·9 cm. (1·3 grm.); *Case* 3, 6·8 × 2·8 × 1·4 cm.; (13·5 grm.); *Case* 4, 7·5 × 5 × 1·8 cm. (26·2 grm.), and 2 × 1·3 × 1·2 cm. The enlargements are, therefore, in all cases very great and obviously far beyond the normal fluctuations in size. In no case, however, do the enlargements appear to be autonomous new growths. They are occupied by cells which, apart from giant nuclei and multiple nuclei, correspond in structure and size to those found in the normal glands of adults (p. 220). Giant and multiple nuclei are not evidence of neoplasm; they are found in abnormal activities of glands, for instance in the thyroid gland in Graves' disease. In *Case* 3, 1930, and *Case* 1, there is in places a hyaline degeneration of the capsule or of the walls of vessels, which is usually complicated by calcification. In *Case* 1 a few parenchymatous cells that are enclosed within the meshes of the net of hyaline calcified vessels are themselves necrosed and calcified. Such retrogressive changes are not, however, proof of neoplasm; degenerative changes are very conspicuous in diffuse colloid goitre. In *Cases* 3 and 4, 1930, and *Case* 3 many irregular and rounded cystic spaces are filled with acidophil coagulum. But these spaces are merely exaggerations of the small spherical spaces containing secretion which are frequently found in normal glands. There is no other abnormality in the architecture of the glands except such alterations in the shape of the acini and the disposition of their reticulovascular boundaries as would necessarily result from enlargement of the acini by hyperplasia of their cells. The predominant type of cell varies in different cases and in different glands in individual cases, suggesting phases of functional activity. In *Case* 3, 1930, ballooned principal cells greatly predominate, and in *Case* 2 they constitute almost all the cells. In *Case* 4, 1930, slightly vacuolated principal cells and pale oxyphil cells are present in about equal numbers. In *Case* 3 almost all the cells are pale oxyphil cells with considerable dropsical separation of their granules. In *Case* 1 dark oxyphil cells greatly preponderate over ballooned principal cells in the smaller gland, but in the larger gland the relations are reversed so that the ballooned principal cells form the bulk of the two glands taken together. In *Case* 4 the larger gland is occupied almost completely by pale oxyphil cells, whilst in the smaller gland small acini of principal cells are clearly in process of conversion into large acini of pale oxyphil cells. The ballooned principal cells contain, as in the normal gland, much glycogen. The pale oxyphil cells contain less glycogen, the dropsical type (*Case* 3, *Fig.* 190) containing more than the more solid type. The evidence that the enlargement is a functional hyperplasia appears to be conclusive in *Case* 4, where the smaller gland shows all stages of conversion of small acini of principal cells into massive acini of pale oxyphil cells similar to the acini that occupy the larger gland.

The evidence appears to be conclusive that the enlargement of the parathyroid glands is due to a functional hyperactivity and not to autonomous

neoplasm. Consequently, if the changes in the bones are the result of excessive secretion of the parathyroid glands, the position is similar to that in Graves' disease, in which the cause of the abnormal activity of the thyroid gland is unknown. Parathyroid hyperplasia is known, however, to occur secondarily to abnormal conditions of the skeleton. It has been seen, for instance, in the disturbance of calcium metabolism constituting osteomalacia (Erdheim, 1907; Hoffheinz, 1925), and in hæmatogenous myelomatosis (Barr and Bulger, 1930; Bulger, Dixon, and Barr, 1930). Further, Klemperer (1923) found hyperplasia of a parathyroid gland in a case of extensive destruction of the skeleton by secondary carcinoma, but he thought that osteomalacia was also present. The view that the enlargement of the parathyroid glands in generalized osteitis fibrosa is secondary to the changes in the bones cannot, therefore, be dismissed without consideration. In focal osteitis fibrosa there is no generalized osteoclastic resorption of the skeleton. The changes, however, in the bone in the areas affected by the focal osteitis fibrosa cannot be distinguished histologically from those in the more severely affected areas in generalized osteitis fibrosa, as is shown by *Case* 8 of this paper. Cysts and osteoclastomata frequently occur. In Paget's osteitis deformans the resemblance to generalized osteitis fibrosa is still greater because the alteration may involve the whole skeleton. Von Recklinghausen (1891), who first described under the name of "fibrous or deforming ostitis" three cases, of which one at any rate (*Case* VII) was a typical example of generalized osteitis fibrosa, considered that his cases were a form of Paget's osteitis deformans. The resemblance is recognized by the two conditions being called respectively osteitis deformans of Paget and osteitis deformans of von Recklinghausen.

In Paget's osteitis deformans there is a similar interplay of excessive lacunar resorption and apposition. Even in cases in which the disease has been conspicuous for years osteoclasts in Howship's lacunæ may be very numerous in parts of the bones. In the descriptions in this paper of the portions of bone removed in generalized osteitis fibrosa stages of reconstruction of the compacta can be traced: porosis is initiated by lacunar resorption of the Haversian canals, whilst continued resorption and apposition lead to conversion of the compacta into a spongiosa that has an entirely new architecture and is composed entirely of bone formed during the disease. In the same way in Paget's osteitis deformans the corticalis of the large tubular bones is converted into a spongiosa of newly formed trabeculæ composed of numerous systems of lamellar bone, and the flat bones such as the sternum and calvaria become spongy throughout. Resorption and apposition also reconstruct the trabeculæ of the spongiosa, but alterations in the architecture of the spongiosa of the long bones are much less conspicuous than in the corticalis. The newly formed bone in generalized osteitis fibrosa consists largely of woven bone. In the more chronic reconstruction in Paget's disease woven bone is very rare. It is found, however, in places in the earlier stages, but is soon replaced by lamellar bone (Schmorl, 1930). There is no evidence of osteomalacia. The resorption and apposition are associated with a fibrosis of the marrow, and this shows the same intimate relation to bone and to the degree of alteration of bony structure that has been described above as characteristic of generalized osteitis fibrosa. This relation is most

conspicuous in the spongiosa of the large tubular bones, where most of the trabeculæ are clothed partially or completely by a zone of fibrous marrow of variable depth; the fibrosis is sometimes confined to a space eroded within a trabecula. The zonal arrangement of the fibrosis can also be recognized in the altered compacta. Engorgement, hæmorrhage, and the accumulation of pigment-granule-cells are again conspicuous. Osteoclastomata are rare; Schmorl (1930) has found none. They do occur occasionally, however. In a typical skeleton (P.M. 944, 1907) from a man of 49, who had noticed the deformities for eight years, an osteoclastoma in the skull had extended into the scalp and had also bulged into the brain. Cysts are also rare. Knaggs (1926) found no evidence in museum specimens, and Schmorl (1930) has not seen them in his abundant material. In the London Hospital Museum, however, there is a left femur in which two superimposed cysts, measuring 2·2 × 1·4 cm. and 2·1 × 1·4 cm., are separated by a narrow partition and lie in the inner part of the shaft immediately below the neck. Their inner ends lie in concavities in the corticalis. This specimen was obtained at necropsy (P.M. 363, 1928) from a typical skeleton in a man of 61 years. Spontaneous fractures are relatively common. There is, therefore, a close resemblance between the histological processes in the osteitis deformans of Paget and in generalized osteitis fibrosa. In generalized osteitis fibrosa, however, resorption greatly exceeds apposition, whilst in Paget's osteitis deformans the two processes are more evenly balanced and apposition exceeds resorption. Further, the processes are less acute in Paget's disease. The long continuation of the two processes side by side in very nearly equal amounts is shown by the bone consisting of an abnormally rich mosaic of very numerous small lamellar systems with eroded margins. To this feature, which I have pointed out in my lectures for many years, my former teacher Professor Schmorl (1930) has drawn particular attention; he considers the great number and the irregular arrangement of the systems to be diagnostic of the disease. In the description in this paper of the portions of bone excised from cases of generalized osteitis fibrosa the number of systems in the bone formed during the disease has been mentioned, and has been used as a measure of the persistence of both processes of resorption and apposition; but where the systems were most numerous their number was small. The preponderance of apposition is shown in Paget's disease by the characteristic thickening and enlargement of the affected bones and the increase in their weight in spite of the porosity of the compacta. In generalized osteitis fibrosa certain bones, for instance the calvaria in *Case* 1, may be greatly thickened and increased in weight, but the bony skeleton is greatly reduced as a whole. In focal osteitis fibrosa, even when the foci are multiple, and in Paget's osteitis deformans there is no chemical evidence of a disturbance of calcium metabolism (Hunter, 1930). The parathyroid glands are not enlarged in Paget's disease (Schmorl, 1930).

It has been shown that the enlargement of the parathyroid glands in generalized osteitis fibrosa is due to functional hyperplasia, that hyperplasia of the parathyroid glands is known to occur secondarily in diseases of bone, and that the abnormal processes in the bones in generalized osteitis fibrosa and Paget's osteitis deformans are closely similar except that resorption

greatly preponderates in the former. Even if the animal experiments of Jaffe and his collaborators are not accepted as conclusive, the abnormal calcium metabolism in patients, the effect of extirpation of their enlarged glands, and the mobilization by parathormone of metals from the skeleton into the blood make it impossible to believe that the secretion from the enlarged parathyroid glands in generalized osteitis fibrosa does not cause a change in the skeleton. In as much as there is no unequivocal evidence that halisteresis occurs in any abnormality of the skeleton, there can be little doubt that this change is a lacunar resorption. It might, therefore, be argued that generalized osteitis fibrosa and Paget's osteitis deformans both begin with one and the same disease of bone, but that in generalized osteitis fibrosa this disease happens to induce secondarily a functional hyperplasia of the parathyroid glands and the additional lacunar resorption due to parathormone causes the difference between the two conditions. But the cause of the changes in Paget's disease is unknown. Arguments have been given above to show that if the cause of the changes in the skeleton in generalized osteitis fibrosa lies within the skeleton, it must lie within bone. These arguments apply equally to Paget's disease. It has, indeed, been suggested that Paget's disease is due to some abnormality in the bony substance. By no histological method, however, has any abnormality been demonstrated (Schmorl, 1930). It would be more reasonable to argue from the known to the unknown. There is definite evidence that parathormone alters the normal equilibrium of the skeleton, and that extirpation of enlarged parathyroid glands improves the condition of the skeleton in patients suffering from generalized osteitis fibrosa. All the available evidence points to excessive parathyroid secretion as the cause of the skeletal changes in this disease. The general resemblance to the abnormal processes in Paget's osteitis deformans suggests that the cause of this disease also lies outside the bone, and is some disturbance of the multiple factors which regulate the formation of bone. If it is accepted, however, that the changes in the skeleton in generalized osteitis fibrosa are entirely secondary to hyperfunction of the parathyroid glands, the cause of that hyperfunction is still unexplained. The position, as already mentioned, is similar to that in Graves' disease. The practical importance of this conclusion is very great, because it makes it impossible to foretell the ultimate results of extirpation of one or two enlarged glands.—H. M. T.

FOCAL OSTEITIS FIBROSA.

Of much more common occurrence than the generalized disease is focal osteitis fibrosa. This is a condition affecting one or more bones, usually not disabling, of slow progress, and showing a tendency to become arrested. It occurs chiefly in adolescence, and is often symptomless until spontaneous fracture occurs. In the descriptions of cases which follow it will be seen that the figures for serum calcium and plasma phosphorus are invariably normal, a finding in striking contrast to that of the generalized disease. The calcium balance is usually normal, and, taken in conjunction with a normal blood chemistry, this finding is of far-reaching importance. Supported as it is by the normal density of the radiographic shadows of bones, it is evidence

strongly against hyperparathyroidism. It is of vital importance in such cases to realize that, although many bones are affected, the condition is totally different from the generalized disease, and that exploration of the neck is usually unjustifiable.

Case 5.—**Osteitis fibrosa in multiple foci.**

O. U., female, aged 18. (L.H. Reg. No. 41679/1928.)

History.—Two years, aching pain in right leg below knee, noticed thickening of right shin. Eighteen months, pain and limitation of movement in right hip. Spontaneous fracture of right femur. After rest in bed for three months good union occurred. Six months, increase in size of swelling on shin with pain. No family history of bone disease.

On Examination.—Well-developed girl. Calvaria normal. Sclerotics white. No exophthalmos. Lenses normal on examination by slit-lamp. Hearing normal. Teeth sound. Slight uniform (adolescent) thyroid enlargement. No other swelling felt in neck. No tachycardia. No limitation of movement of hips or other joints. Slight thickening but no bowing of subcutaneous surface of right tibia in its middle third. Urine normal. Wassermann reaction negative.

Radiograms.—Pale cyst-like areas in upper two-thirds of shaft of right femur and in middle third of shaft of tibia, the latter expanding the corticalis. Controlled radiograms showed that outside these areas the shadows of all bones examined were of normal density. Calvaria normal. No calculi in renal tract (Dr. S. G. Scott).

The blood chemistry was examined at intervals over a period of two years and found repeatedly to be normal (serum Ca 9·9 mgrm. per 100 c.c., plasma P 3·5 mgrm., plasma phosphatase, 0·248 mgrm.). On a known low calcium intake the calcium output in urine and fæces was normal (*Fig.* 180).

Case 6.—**Focal osteitis fibrosa of right humerus.**

R. N., male, aged 13. (L.H. Reg. No. 31663/1930.)

History.—Two years ago while running he slipped and fell backwards hurting his right shoulder. Humerus immobilized for four days in plaster jacket. Treated subsequently by massage. Three months, occasional sharp pain at point of right shoulder, unrelated to movement and with no radiation. No pain elsewhere. No family history of bone disease.

On Examination.—Thin, rather small boy. Calvaria normal size and contour. Sclerotics white. Lenses normal on examination by slit-lamp. Hearing normal. Teeth good. No tumour felt in neck. No abnormality of skeleton detected. Urine normal. Wassermann reaction negative.

Radiograms.—Pale area with multiple trabeculæ expanding corticalis in upper third of right humerus. Controlled radiograms showed that outside these areas the shadows of all bones examined were of normal density. Calvaria normal. The renal tract showed no calculi.

The blood chemistry was found repeatedly to be normal. (Serum Ca 10·0 mgrm. per 100 c.c., plasma P 3·8 mgrm., plasma phosphatase 0·379 mgrm.) On a known low calcium intake the calcium output in urine and fæces was normal (*Fig.* 180).

Case 7—**Osteitis fibrosa in multiple foci.** (Hunter, 1930, *Case* 5.)

L. R., married woman, aged 27. (L.H. Reg. No. 40007/1930.)

History.—Twelve months, enlargement of right arm above elbow. Three weeks, aching pain in arm began in fourth month of pregnancy. No fracture or history of fracture. No family history of bone disease. Two children well.

On Examination.—Well-nourished, small woman. Calvaria normal. Sclerotics white. No visual defect. Slit-lamp examination showed within the fœtal nucleus of each lens crowds of tiny white glistening dots surrounded by a small area of cloudy lens (Mr. C. Goulden). Hearing normal. Caries of three teeth. No tumour

felt in neck. Diffuse irregular enlargement of right humerus with outward bowing in upper part. No deformity of other bones. Urine normal. Wassermann reaction negative.

Radiograms.—Right humerus and radius show pale trabeculated areas with expansion of bone. Similar, less definite, areas round acetabulum and in left ischium. Controlled radiograms showed that outside these areas the shadows of all bones examined were of normal density. Calvaria normal. The renal tract showed no calculi (Dr. S. G. Scott).

The blood chemistry was found repeatedly to be normal (serum Ca 9·8 mgrm. per 100 c.c., plasma P 3·0 mgrm., phosphatase 0·363 mgrm.). On a known low calcium intake the calcium output in urine and fæces was normal (*Fig.* 180).

Case 8.—**Osteitis fibrosa in multiple foci.**

G. B., male, aged 12. (L.H. Reg. No. 31553/1930.)

History.—Two years, pushed on to curb-stone, broke left arm. Treated for fracture of left radius by splinting and massage. Twelve months, mother noticed that he limped with the right leg and she found right thigh bowed outwards.

Past History.—Lump on back of head for years. Never had rickets. No history of polydipsia, polyuria, renal pain, or passage of stone or gravel. No family history suggesting disease of bones.

On Examination.—Well-built boy. Abnormal prominence of left side of occipital bone and of left parietal eminence. Sclerotics white. Lenses normal on examination by slit-lamp. Hearing normal. Teeth good. No tumour felt in neck. Right femur bowed outwards and forwards; right leg 1·5 cm. shorter than left. Thickening of second phalanges of third and fourth digits of left hand. No tenderness of bones on pressure. Heart, lungs, abdomen, and nervous system normal. Trousseau and Chvostek signs absent. Urine normal. Wassermann reaction negative.

Radiograms.—Shadow in left parieto-occipital region suggests osteoma. Bowing of right femur with new bone formation along inner aspect and pathological fracture through thinned, irregularly mottled outer aspect. Left radius, left humerus and metacarpals, and most phalanges of left hand show pale irregular shadows with slight expansion of the corticalis suggesting osteitis fibrosa. Controlled radiograms show that outside these areas the shadows of all bones examined are of normal density. No renal calculi (Dr. G. E. Vilvandré).

Operation (Mr. R. Milne—July 14, 1930).—Wedge-shaped osteotomy of right femur performed through middle of antero-lateral aspect of thigh. Alignment of limb corrected; right hip immobilized in plaster-of-Paris.

Pathological Report.

(Professor H. M. Turnbull.)

Tissue removed at operation. (S.D. 1626/1930.)

1. **Right Femur.**—

Macroscopic.—The specimen was a wedge-shaped segment (3 × 2 × 2 cm.) of the whole cross-section of the shaft. It had been placed in formaldehyde. The cortical surfaces, where not covered by periosteum, were grey and beset with longitudinal sulci that were just visible to the naked eye. On the cut surfaces the inner and outer corticalis formed zones (up to 2 mm. deep) of homogeneous grey bone interrupted by a few small pink dots and streaks. Between these was a dense, gritty, cancellous bone in which a net of slender grey trabeculæ, enclosing small pink spaces, was just visible to the naked eye. The spaces tended to have their long axes parallel to the cortical surfaces.

Microscopic.—The wedge was fixed and extensively decalcified by alternate immersions in 4 per cent formaldehyde in distilled water (pH 3 to 4) and Müller's fluid, followed finally by thirty minutes in 5 per cent nitric acid.

A narrow layer of corticalis occupies both the base and the apex of the wedge. It has a spongy texture owing to large medullary spaces occupied by fibrotic marrow. On one side a portion of tendon replaces the periosteum and beneath this are areas of woven coarse-fibred bone and, rarely, of calcified fibrocartilage. The rest of this cortical layer consists of lamellar bone. Recent resorption is shown by many large osteoclasts in Howship's lacunæ upon the walls of some of the medullary spaces. Recent apposition is shown in several places by osteoblasts upon osteoid zones. Extending from one corticalis to the other is a close mesh of slender bony trabeculæ in a fibrotic marrow (*Fig.* 188). The trabeculæ are composed of woven bone, but near the corticalis a few contain small portions of lamellar bone. Many trabeculæ are formed by more than one system of woven bone. Recent resorption is shown throughout by many large osteoclasts in lacunæ, and past resorption by numerous lacunæ beneath osteoid zones. Apposition is, however, at present greater than resorption. It is very active, the osteoblasts being very numerous and large. The osteoid zones in general appear to be very deep (*Fig.* 188). This is due largely to frequent obliquity of section. Where cut at right angles to their surfaces the zones are not deeper than in actively healing fractures. The marrow in the medullary spaces of the corticalis and medulla consists of numerous spindle and stellate fibroblasts in a matrix of closely packed collagen fibrils. The fibroblasts are very uniform in morphology; variations in the density of the fibrosis are slight; the vessels have walls of normal structure and are not dilated.

Remarks.—Resorption has led to the disappearance of almost all the original bone except a narrow outer strip of corticalis, and has converted this from compact bone into spongy. In the rest of the bone resorption and apposition have replaced lamellar bone by a woven bone, and have completely altered the architecture. The new spongiosa is of much closer texture than the normal and the medullary cavity has been obliterated. Long duration of abnormal conditions is shown by many trabeculæ containing a mosaic of separate systems of woven bone. These changes are associated with a dense but cellular fibrosis of the marrow. There is no evidence of a cessation of calcification of osteoid tissue, that is, of osteomalacia. The general picture is that of an osteitis fibrosa. The changes cannot be differentiated from those in the osteosclerotic areas in generalized osteitis fibrosa—for instance, in the skull in *Case* 1 (*cf. Figs.* 188 and 187).—H. M. T.

Subsequent Progress.—The patient was sent to a convalescent home and later re-admitted for further investigation.

Calcium and Phosphorus Metabolism.—The serum calcium was constant within very narrow limits, the average figure for eight estimations being 10·4 mgrm. per 100 c.c. The corresponding figure for plasma phosphorus was 3·5 mgrm. Nevertheless the plasma phosphatase figure was always high, the average for six estimations being 0·912 mgrm. The calcium output was estimated in the urine and fæces for three three-day periods. The patient was kept on a weighed diet of known low calcium content. The calcium output in the urine was about twice the normal, that in the fæces being also about twice the normal (*Fig.* 180).

Operation (Mr. E. C. Lindsay—Oct. 22, 1930).—Under open anæsthesia collar incision made in neck. Sternomastoid muscles were retracted on either side and pretracheal muscles divided. Superficial lymphatic gland removed for section. Thyroid gland apparently normal. Three normal parathyroid bodies identified, left superior not seen. No parathyroid tumour discovered after extensive search. Wound closed. A portion of bone was removed from the lower end of the left radius.

Pathological Report.

(PROFESSOR H. M. TURNBULL.)

Tissues removed at operation. (S.D. 2428/1930.)

1. Left Radius.—

MACROSCOPIC.—A longitudinal slice 2·6 cm. long and 0·6 cm. deep in the centre. The outer surface was covered with periosteum. The cut surface showed a hard white sheet of corticalis, too shallow to be measured, and beneath this a deep red, gritty, and granular tissue in which a spongy texture was just recognizable.

MICROSCOPIC.—The specimen was decalcified completely almost throughout by Müller's fluid followed by nitric acid.

The corticalis has been reduced to a shallow shell, which is split in most of its extent into two layers by a row of long medullary spaces directed in the long axis of the bone. It consists of lamellar bone (*Fig.* 197). Beneath it is a spongiosa formed entirely of woven bone (*Fig.* 198) which is usually coarse-fibred in the centre of the trabeculæ and of intermediate type in the periphery. The trabeculæ are more slender and form a slightly closer net than in the bone removed at the first operation. Further, they show very few separate systems. Otherwise the appearances throughout are very similar. As before, there is much active resorption by osteoclasts, but apposition greatly preponderates. The edges of the bone beneath the osteoid zones are beset with lacunæ. The osteoid zones taken as a whole are very conspicuous, but where they are cut at right angles to their surface the depth is not excessive in view of the activity and the type of bone-formation. The marrow shows a similar fibrosis.

Remarks.—The changes are similar to those in the first piece of bone, but the abnormal changes appear to have been present for a shorter period, the trabeculæ of woven bone showing very few separate systems. The changes are such as are found in osteosclerotic areas in examples of generalized osteitis fibrosa.

2. Lymphatic Gland.—The gland measured 1·3 × 0·7 × 0·4 cm., and its lymphatic nature was confirmed by microscopic examination.—H. M. T.

Remarks.—The points against hyperparathyroidism in this case are the normal serum calcium and plasma phosphorus together with the absence of evidence of osteoporosis in controlled radiograms. The high calcium output and high plasma phosphatase are probably expressions of the destruction of bone in multiple foci. Future estimations of calcium metabolism in this case will afford information of great value. It is not known whether in such cases hyperparathyroidism ever develops.

OSTEOMALACIA.

Morbid anatomists are agreed that in rickets and osteomalacia the essential abnormality is the same—namely, a deficient calcification of osteoid tissue. This deficiency is generalized throughout the skeleton. In rickets, since endochondral ossification has not ceased, the zone of provisional calcification is affected too, and endochondral ossification is irregular.

The nature of the calcium deficiency has given rise to much controversy. Virchow (1853) held the view that calcium salts had been removed from calcified bone, leaving osteoid tissue. This was the doctrine of 'halisteresis',

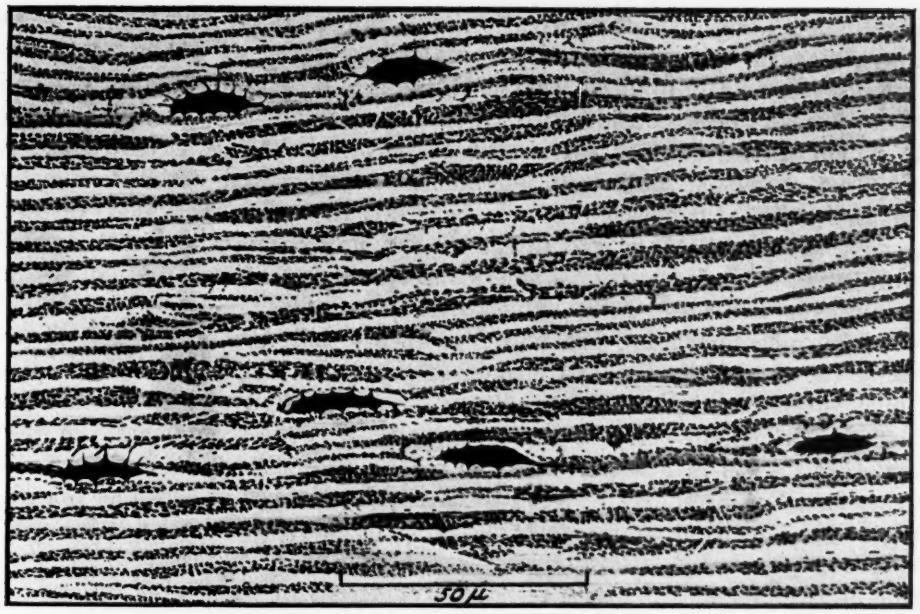

FIG. 197.—*Case* 8. Left radius. Osteitis fibrosa in multiple foci. Müller's fluid followed by nitric acid ; Schmorl's thionin-phosphotungstic-acid method for fibrils. Lamellar bone in outer remnant of compacta of corticalis.

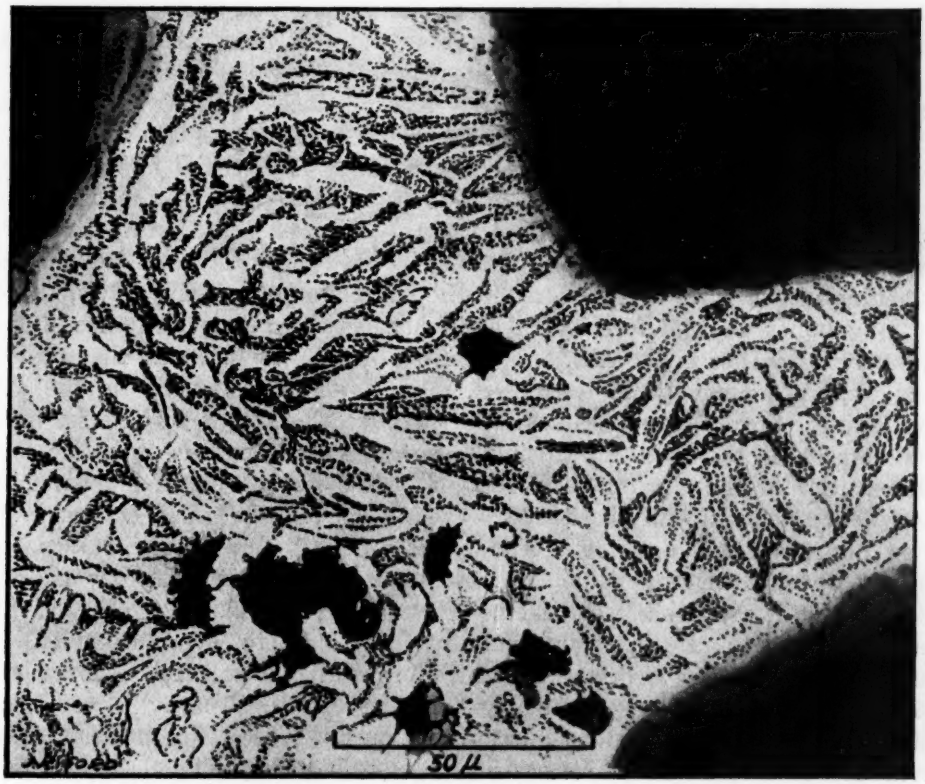

FIG. 198.—*Case* 8. Left radius. Osteitis fibrosa in multiple foci. Müller's fluid followed by nitric acid ; Schmorl's thionin-phosphotungstic-acid method for fibrils. Trabecula of woven, coarse-fibred bone in newly formed, spongy corticalis beneath.

which means literally 'salt deprivation'. Pommer (1885) and Schmorl (1909), while expressing the view that osteomalacia and rickets are essentially the same disease, held in addition that halisteresis is not responsible for the broad osteoid zones. They considered that, in both diseases, the calcifying mechanism which should convert osteoid tissue into true bone was deficient. Not only does any bone added by advancing endochondral ossification remain osteoid, but so also does all new bone added to trabeculæ which were fully calcified at the onset of the disease. The normal physiological resorption accompanies this apposition, and consequently portions previously hard become ever softer and more liable to bend.

Now, although there are many problems still unsolved concerning the etiology of these two diseases, it is clear that the calcifying substance which is missing is vitamin D. In its absence the utilization of calcium and phosphorus is impaired. In the majority of cases of osteomalacia the serum calcium is low as in low-calcium rickets. In both diseases the abnormalities in the blood are promptly restored to normal by the use of cod-liver oil, ultraviolet light, or irradiated ergosterol. At the same time ossification begins to proceed normally. Biochemistry has therefore amply justified the view held by Pommer and Schmorl of the pathogenesis of these diseases and their essential identity.

Clinical Features.—Osteomalacia is a deficiency disease endemic over wide areas in Northern India, Japan, and Northern China, and occurring sporadically in the Rhine Valley, Danube Valley, Vienna, and certain parts of Italy, Switzerland, Flanders, and the Balkans. It is a rare disease in the British Isles and U.S.A. It pre-eminently affects women, and is likely to recur earlier and with greater severity in each successive pregnancy. Many cases clear up after lactation is complete, or even before this time. However, it is a mistake to suppose that pregnancy is essential in its etiology; it is sometimes seen at puberty, and is quite well known to occur, though it is rare, in boys and men (Wilson, 1931). Maxwell (1923) states that it is known to the Chinese as 'Yao t'ui t'eng'—'back-and-thigh pain'. The pain is aching in character and is worse in the winter months. The pelvis, thorax, or long bones show deformity in a haphazard way; one woman suffers in the pelvis, another in the ribs, and a third in both. Besides the characteristic and well-known change in the pelvis, marked deformities occur in the chest and spine. Severe kypho-scoliosis may reduce the height by several inches and cause the head and neck to sink downwards and forwards on to the chest. Deformities of the sternum and ribs may give rise to marked prominences and depressions in the chest wall. Coxa vara and irregular curves in the long bones are less common. The bones are soft and flexible rather than fragile, so that bending is much more common than spontaneous fracture, though both are well recognized. The patient develops a characteristic waddling gait, and muscular weakness may add to her incapacity. In many cases the pelvic deformities interfere with marital relations or with labour, Cæsarean section frequently being necessary. Tetany is very common, and the attacks may last for hours. Wilson (1931) has found evidence of osteomalacia in cases of the so-called idiopathic tetany or 'wai' of Kashmir.

Pathogenesis.—It is only in recent years that real progress has been made towards solving the problem of the etiology of this condition. For almost half a century the hypothesis was held that the disease was due to a pathological increase in the activity of the ovaries leading to hyperæmia of the bones and a consequent solution of their lime salts. This was not based on accurate experiment, neither was there any evidence worth the name that the ovaries were histologically abnormal. The hypothesis arose in 1879 when Fochier performed Cæsarean hysterectomy in several cases of osteomalacia and found that a good effect was produced on the progress of the disease. Fehling (1884) performed ovariotomy for osteomalacia quite apart from pregnancy, and within a few years this treatment was performed all over the world. Now, while there can be no doubt that pregnancy leads to the development of osteomalacia, there is very little evidence that the ovaries exert any effect on the disease apart from their rôle in pregnancy. Castration presumably acts by stopping the possibility of further pregnancy and lactation with their consequent drain on skeletal calcium, and this can be as easily done by ligature of the Fallopian tubes.

An amazing fallacy regarding the etiology of osteomalacia originated in the work of Bossi (1907), who arrived at a method for treating the disease with adrenalin by the following argument: "Since suprarenal substance is known through its pressor action to modify deeply the circulation in both sexual organs and bone-marrow, since removal of the suprarenal has been shown in animals to cause deep and lasting changes in the ovary, I thought of treating this case with suprarenal substance (adrenalin)." After claiming, on quite inadequate evidence, that the patient was cured by the injections, he proceeded to an experiment upon a sheep in the middle of pregnancy. He removed one suprarenal and the animal remained well until the seventh day, when it had difficulty in walking. On the eighth day it could neither stand nor walk, and it showed "curvatures of the joints in the whole body, the hips markedly rotated inwards, and painful on pressure". Such is the evidence on which the suprarenal origin of osteomalacia is based. One asks oneself whether its exponents of to-day have troubled to read the article from which it sprang!

Studies of the mineral metabolism of osteomalacia date back many years, and began with analyses of the bones. McCrudden (1910) in a case of adolescent osteomalacia found 15·4 per cent CaO in dried bone as compared to 28·8 per cent in normal bone. In 1910 the same observer demonstrated a negative calcium balance in eight cases of osteomalacia.

The blood chemistry had not been studied accurately until Miles and Feng (1925) investigated ten patients. These cases varied in duration from eight months to twenty years; in seven there was tetany, and in all a considerable diminution in the serum calcium (5·0 to 7·4 mgrm. per 100 c.c.). The plasma phosphorus varied from 1·8 to 3·8 mgrm. per 100 c.c. The same workers carried out calcium balance experiments on four adult females taking a low calcium diet consisting of millet gruel, wheat bread rolls, celery-cabbage, garlic, and dry steamed millet. A negative calcium balance was found in three patients, positive in one. Keeping the diet identical and adding cod-liver oil, alone or in combination with either calcium lactate or calcium

phosphate, they were able to bring about marked retention. In one patient receiving olive oil with calcium lactate, the calcium balance remained negative. Osteomalacia therefore chemically resembles low calcium rickets. In the present state of our knowledge the occurrence of hyperplasia of the parathyroids in osteomalacia (Erdheim, 1907) is without explanation. Since all the parathyroids are usually affected, the hypothesis that the change is compensatory seems attractive.

Economic Factors Responsible for Osteomalacia.—With the story of rickets before us we can trace the economic factors operating in the causation of osteomalacia. They are factors difficult for a Western civilization to appreciate, deep-rooted as they are in the social and religious customs of the East. The diet of the Chinese people is meagre, consisting, as in the experimental diet used by Miles and Feng, entirely of cereals and a limited amount of vegetables with no milk, meat, or eggs. It is deficient in vitamin D and in calcium salts, and contains an excess of acid-forming over base-forming mineral elements. The environment tends to keep the woman patient isolated from the sun, for foot-binding retards movement, and the severe winters of the high plateau of North China lead to confinement indoors. When the pains of osteomalacia begin she retires to her warm brick bed, thereby completely shutting herself off from the sun. In India the areas affected are in the north, in the high valleys where sunlight is scanty in winter owing to the surrounding mountains. As in China, there is a marked seasonal incidence, the disease being worse in winter and early spring. In Kashmir the disease is worse in the cities. There are narrow courtyards and the houses have a minimum of window space. The women affected are those observing strict purdah (Vaughan, 1926). They are systematically screene from the sun from the age of ten. No cases are seen in Kashmiri boat women who live in the open air and drink milk provided by a goat or a cow carried in the boat. Nevertheless, Wilson (1931) has observed in the Kangra district of the Punjab severe osteomalacia in women who work in the open air where sunshine is plentiful for eight months of the year. The diet of these women is grossly inadequate and contains no milk or eggs. In many places in India no raw fruit or vegetables are eaten, largely from fear of cholera. The pregnant woman is kept short of food with the idea of keeping the fœtus small for an easy labour. The calcium drain of lactation is very severe, for it commonly continues as long as four years. Under such social conditions it is not surprising that other deficiency diseases may exist together with osteomalacia. Thus Wampler (1924) reports œdema in one-third of forty-six cases, and xerophthalmia in one.

Treatment.—In the treatment of osteomalacia, as in the case of rickets, cod-liver oil, sunlight, and irradiated ergosterol each has its place. Vaughan reports that "out-patients given cod-liver oil and ordered to go out on the lake in open boats improved rapidly." Starlinger (1927) and Hottinger (1927) report cures with irradiated ergosterol, and it is an interesting fact that each of their cases had been previously treated unsuccessfully by ovariotomy. Maxwell states that "given cod-liver oil, good food, and sunlight, the majority of the patients will slowly recover. Cod-liver oil and calcium salts quickly remove tetany and the worst of the pain." He finds that some

cases require 1½ oz. of cod-liver oil with 1 mgrm. of irradiated ergosterol daily. But he adds, " we want flocks and herds, milk and meat, with security of life and property."

Case 9.—**Osteomalacia.**

E. R., married woman, aged 33. (L.H. Reg. No. 40829/1930.)

Obstetric History.—Catamenia commenced at 13 and were regular. Married 15 years.

1916.—Full term pregnancy, normal labour. Girl, now 14.

1918.—Full term pregnancy, normal labour. Girl, now 12.

1919.—Full term pregnancy, normal labour. Male child; died in convulsions a few days after birth.

1922.—Full term twin pregnancy, normal labour. Boy, now 7. Girl died 17 days after birth, in convulsions.

1923.—Full term twin pregnancy, difficult labour, instrumental delivery. Intranatal death of girl. Boy survived three months, then wasted and died in convulsions.

The three babies who survived were breast fed for twelve months.

History.—1922.—Immediately following fourth pregnancy began to have pains in left hip and back. Limped with left leg. Pains in ankles.

1923.—During last month of fifth pregnancy pains in limbs recurred. Vomiting. Was in bed three months with swelling of left leg. Aching all over, especially in lower part of spine. When allowed up could only get from chair to chair with difficulty.

1925.—She was thought to suffer from tuberculosis of the spine, but when radiograms were taken she was told that the condition was osteomalacia, the 'pelvic diameter' being 1½ in. In bed six months in order to straighten out the bones. Pain in bones on shaking hands.

1926.—Treated with ultra-violet rays and thyroid tablets. Took the tablets twice a day for twelve months, and then her husband made her give them up because her bones were worse; often in bed with pains in bones. From this time husband had to look after house and children.

1928.—Diminution of two inches in total height. Arms and legs tender on deep pressure. Bowing of right forearm. Unable to walk unaided. Able to get about by resting arms on a wheel chair. Five teeth extracted for apical abscesses.

Six months.—Slight bowing of left forearm. Severe aching pains in bones. Muscular weakness, especially in back.

Past History. — Born in Darlington, Durham, and has always lived there. Did not suffer from rickets as a baby. Good teeth as a child, first extractions at fourteen for apical abscesses. Has always taken normal food; no idiosyncrasies in regard to diet. No history of having passed gravel or stone. No increased frequency of micturition. No history of fractures nor tetany. No family history suggesting disease of bones.

On Examination.—Height, 4 ft. 4 in. Weight, 7 st. 1 lb. Well-nourished woman. Acne rosacea. Able to stand unaided, but requires assistance to walk. Calvaria normal size and contour. Sclerotics white. Lenses normal on examination by slit-lamp. Hearing normal. Double dentures, recession of gums of remaining lower teeth. Tongue clean. Mucous membranes normal colour. No tumour felt in neck. Heart and lungs normal. Blood-pressure 115/85 mm. mercury. No abnormality in nervous system. Trousseau and Chvostek signs absent. Stooping attitude with slight kyphosis and sinking of chin towards chest. Angulation forwards and central thickening of both clavicles. Considerable bowing of right forearm. Thorax sunken towards pelvis; transverse crease in abdominal wall. Genu valgum; when the internal condyles of the femora are approximated the internal malleoli are separated by a distance of 4½ in. Tenderness on pressure upon long bones and ribs. Points of maximum tenderness, for example, in lower end of right radius and upper end of left fibula. No bone tumours felt. Pelvic measurements: interspinous, 25·4 cm., intercristal, 28 cm., external conjugate, 16·5 cm., transverse diameter at outlet, 2·5 cm., promontory not reached by examining finger.

Urine.—Acid; sp. gr., 1022; no albumin; no sugar. Bence Jones protein absent.

Blood.—Red cells, 5,400,000. Hb, 85 per cent; C.I., 0·78; leucocytes, 7000; differential count, normal. Wassermann reaction negative.

Fractional Test-meal.—Complete achlorhydria. Total acidity, 10. Slow rate of emptying.

Fat in fæces: total, 37·4 per cent; unsoaped, 12·7 per cent.

FIG. 199.—*Case* 9. Osteomalacia. Controlled radiogram of left forearm.

Radiograms of Bones (June 5, 1930).—Spontaneous fractures, with no displacement, in shafts of right femur, right fibula, left radius (*Fig.* 199), in both ulnæ, and in 6th, 7th, 9th, and 10th left ribs. Pale cyst-like areas in right tibia and fifth left metacarpal, with no expansion of corticalis. Calvaria shows innumerable pale rounded mottled shadows many of them more than 1 cm. in diameter (*Fig.* 200). Greatly deformed tri-radiate pelvis with fracture of superior ramus of os pubis on each side (*Fig.* 202). In a lateral view the thoracic and lumbar vertebræ show

FIG. 200.—*Case* 9. Osteomalacia. Radiogram of skull before treatment.

FIG. 201.—*Case* 9. Radiogram of skull after treatment.

considerable bi-concave deformity. By contrast with the bones of a control subject the right femur, tibia, humerus, radius, ulna, and hand, as well as other bones, show definite diminution in density (*Fig.* 199).

Radiograms of renal tract show no calculi.

Calcium and Phosphorus Metabolism. — Observations were made upon the blood chemistry at intervals over a period of eleven months. Before treatment the serum calcium varied between 9·6 and 10·1 mgrm. per 100 c.c., and the plasma

FIG. 202.—*Case* 9. Osteomalacia. Radiogram of pelvis.

phosphorus was constantly 1·5 mgrm. per 100 c.c. Plasma phosphatase 1·2 mgrm. The calcium output was estimated in the urine and fæces for three three-day periods, the patient being kept on a weighed diet of known low calcium content. The calcium output in urine and fæces was slightly less than in the control (*Fig.* 180).

PROGRESS.—A portion of bone was removed for histological section.

OPERATION (Mr. R. Milne, July 7, 1930).—A piece of bone was removed from the inner aspect of the right tibia. Periosteum, corticalis, and a portion of spongiosa were included.

Pathological Report.

(PROFESSOR H. M. TURNBULL.)

Tissue removed at operation. (S.D. 1573/1930.)

Tibia.—

MACROSCOPIC.—The specimen was a longitudinal slice from the inner aspect of the tibia. It was 10·5 cm. long, 0·5 cm. deep at each end, and 1 cm. deep in the centre. Beneath the periosteum was an apparently homogeneous corticalis, about

0·25 cm. deep, and beneath this a spongiosa of thin trabeculæ. The spongiosa contained pale yellow, almost white marrow.

Microscopic (*Fig.* 195).—The bone was divided into three pieces and these were decalcified in 4 per cent formaldehyde in distilled water, Müller's fluid, and, finally, nitric acid. The decalcification is not complete. In large areas Kossa's reaction is positive. A control is thus obtained to the estimation by hæmatoxylin-staining of previous calcification in other areas. The periosteal surface is indented by numerous bays, some of which communicate with medullary spaces. The outer fifth of the bone is relatively compact, but has a spongy structure (*Fig.* 195) owing to numerous medullary spaces, which are directed for the most part in the long axis of the bone. There are very few Haversian canals; such as are present are usually wide. In the inner four-fifths the medullary spaces are much larger, so that the bone forms a spongiosa of wide mesh. There are a few small external fundamental systems and several interstitial systems of woven bone; all the rest of the bone is lamellar. There is an osteoid zone on almost all the free surfaces of the bone. Some zones are very narrow, but most are abnormally conspicuous. They are very wide where they have been cut tangentially. Measurements of those that appear to have been cut at right angles to their surfaces show that many are twice as deep as the deeper zones in the bones of healthy infants. Others are much deeper. Some are shown by embedded cells to be composed of two or even three lamellæ. There are also still deeper osteoid zones which in places show ill-defined patches of granular calcareous impregnation. Such patches of partial calcification usually lie in the osteoid zone where it meets the fully calcified bone, but they sometimes lie nearer its centre. The osteoblasts form a single line of narrow cells with very scanty cytoplasm, and they are frequently at a wide distance from one another. In these respects they appear to be less active than in normal infants. An osteoclast in a Howship's lacuna was found after a search through several sections. Some of the osteoid zones lie upon surfaces showing lacunar resorption; they are more often separated from such surfaces by a calcified lamellar system of which they form part. The shallower subperiosteal bays contain a cellular fibrous marrow. All the other spaces contain an adipose marrow, which contains a few hæmatogenous cells in one or two places.

Remarks.—Osteoid zones are present on almost all surfaces. They are exceptionally numerous and exceptionally deep for a healthy adult. Many are twice as deep as the zones in the active growth of early childhood; others are much deeper. Many of the zones are, therefore, deeper than those in the examples of osteitis fibrosa already described, in which the depth was within the limits measured in healing fractures. In osteitis fibrosa and healing fractures the increase in depth beyond that in healthy infants depends upon the greater rapidity of apposition. Rapidity of apposition can be gauged approximately by the size and number of the osteoblasts. If there were very numerous and large osteoblasts upon the zones in the present case, it would be difficult to be certain that the unusual depth was not due to unusual rapidity of apposition, because the depth is seldom conspicuously greater than in healing fractures. The number and shape of the osteoblasts, however, shows that apposition is proceeding very slowly or is in abeyance. The abnormal depth of the osteoid zones and their occasional patchy and powdery impregnation with calcium salts are due, therefore, to complete and partial cessation of their calcification, though a chemical removal of calcium salts from them cannot be excluded on purely histological grounds. In either case the abnormally deep osteoid zones here are definite evidence of osteomalacia.

The osteomalacia is associated with great osteoporosis. As no skeletal

deformities were noted in the childhood of the patient it can be assumed that a compact corticalis was formed in due course, and that the present porosity is due to lacunar resorption. The perfect lamellar structure of the bone that remains suggests that a compact corticalis had been present in adult years. There is extremely little evidence of lacunar resorption at the time of removal of the specimen: only one osteoclast in a Howship's lacuna was found on searching several sections. Surfaces eroded by lacunar resorption are either covered by an osteoid zone, or, more often, by an osseous lamellar system continued by an osteoid zone. Much of the resorption, therefore, has preceded the present attack of osteomalacia.—H. M. T.

Subsequent Progress.—The patient was given a diet of high calcium content, together with 15 grm. of calcium lactate and two tablets of radiostol (British Drug Houses) daily. She was sent home to continue this treatment. Two months after commencing it she became pregnant. She then continued to take the high calcium diet and the calcium lactate but reduced the daily dose of radiostol to one tablet. In spite of the pregnancy and of morning sickness she made rapid clinical improvement. Within three months the pains disappeared from the bones and she began to walk. Within six months she was able to get about the house, to climb the stairs unaided, and to do many household duties such as ironing and baking bread. At this time she was re-admitted to hospital for further investigation. The clinical improvement was fully borne out by the physical examination. Radiograms of the bones (Jan. 13, 1931) showed union of many of the fractures and complete healing of the defects in the calvaria (*Fig.* 201). In spite of these facts the plasma phosphorus was still constantly low, namely, 1·0 mgrm. per 100 c.c. Serum calcium 10·9 mgrm. per 100 c.c. Plasma phosphatase 0·44 mgrm. The dose of radiostol was increased to three tablets daily and ultra-violet irradiation was commenced. Within four weeks the serum calcium rose to 13·7 mgrm. per 100 c.c., but the plasma phosphorus remained low, namely, 1·8 mgrm. per 100 c.c. The patient was sent home on a high calcium diet without radiostol. Except for morning vomiting she remained well, free from pain and able to do her housework. She was finally re-admitted eleven months after treatment was first commenced. At this time the pregnancy was approaching full term. The serum calcium was 13 mgrm. per 100 c.c. In the thirty-sixth week of pregnancy Cæsarean section was performed, together with sterilization by partial excision of the Fallopian tubes. A live female child weighing 5 lb. 4 oz. was delivered. At the operation the pelvic measurements were taken.

Symphysis pubis to promontory 5·9 cm.
Right ileopectineal line to promontory 3·8 cm.
Transverse diameter at brim 9·5 cm.
Distance between nearest points on ileopectineal lines 3·8 cm.

The mother remained well, the low plasma phosphorus and high serum calcium persisting. The baby gained weight, and controlled radiograms of its bones showed no evidence of rickets.

Remarks.—This case is one of 'low phosphorus' osteomalacia. The liability to spontaneous fractures in this type of the disease has been pointed out by Maxwell (1929). The diagnosis is based on the clinical picture, the histology of the bone, the blood chemistry, and the calcium balance. Over a long period the serum calcium was high and the plasma phosphorus low. Under such circumstances confusion with hyperparathyroidism is avoided by determining the calcium balance, thereby demonstrating the absence of an increased excretion of calcium. Confusion may equally be avoided by removing a portion of bone for histological section. The remarkable clinical and

radiological improvement in spite of the pregnancy shows that the absence of vitamin D must be a potent factor in the causation of osteomalacia. It is not necessarily the sole factor.

For his inspiration and example no less than his expert collaboration in pathology I have to thank a great master, Professor H. M. Turnbull. It is also a pleasure to thank Miss Simmonds and her staff for their valuable work both in nursing and dietetics, and I am indebted to Mr. A. J. Walton for the courage and skill of his operative technique. I most gratefully acknowledge the assistance received from Dr. F. B. Byrom in carrying out the animal experiments. My thanks are due to at least fifty other friends and colleagues, only a few of whom are mentioned in the text.

For grants received at various times towards the expense of this work I have to thank the Yarrow Fund of the London Hospital Medical College, the Thomas Smythe Hughes Medical Research Fund of the University of London, and the Ella Sachs Plotz Foundation.

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THE SURGICAL TREATMENT OF PARATHYROID TUMOURS.

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Only a few years ago the anatomy of the apparently insignificant parathyroid glands was hardly known, and in fact many believed that they consisted only of misplaced portions of thyroid tissue or of small lymphatic glands. The appreciation of the fact that injury of these bodies in the operation of partial thyroidectomy might lead to the onset of tetany has of recent years directed considerable attention to their exact situation. More extensive work upon calcium metabolism, of which that of Dr. Donald Hunter in this country is so brilliant an example, has demanded even more detailed knowledge of their normal and abnormal situations. The glands are so small and so hidden away that the diagnosis of a parathyroid tumour depends almost entirely upon indirect evidence. In all four of our cases there were no physical signs of a tumour in the neck. The careful investigations of Dr. Hunter upon the bone changes and upon the calcium and phosphorous metabolism enabled him, however, to say dogmatically that a tumour was present. This becomes a matter of great importance, for in one of our cases the tumour could not be found at the first operation, and I am certain that in a not inconsiderable number a similar failure has occurred elsewhere. Fortunately in our case Dr. Hunter was so certain of the presence of a tumour that a second operation was undertaken, whereby not only was it found but knowledge was obtained which I hope will be sufficient to prevent similar tumours being overlooked in the future.

The number and position of the parathyroids is variable, but as a general rule there is a superior and inferior body on each side, although in many cases these may be increased to three or four. The wide variation of the position of these bodies is shown in Halstead's figure, based upon the investigation of 67 cases of McCullum, which is reproduced in de Quervain's work on goitre. This shows that they occupy a relatively wide strip on the posterior border of the thyroid gland extending from the upper to the lower poles. According to de Quervain they lie in this position between the thyroid capsule and the thyroid fascia, a position which is clearly represented in de Quervain's diagram. The superior bodies may be placed somewhat far forward, and receive, according to Curtis, their blood-supply from branches of the superior thyroid artery. Lahey, who states that one or more parathyroids are not infrequently removed during the operation of partial thyroidectomy, finds that it is on the upper pole especially that this accident is likely to happen. In all my own cases, and in all the post-mortem specimens that I have been able to examine, the superior bodies, although variable in their

lateral and vertical positions, have always been placed anterior to the thyroid fascia and between it and the thyroid capsule.

The inferior glands are placed in close relationship to the inferior thyroid artery, from which—also according to Curtis—they obtain their blood-supply. They may be placed at a very varying level, and in their lower positions come into close relationship with the inferior thyroid veins, where they are more liable to injury. They are usually, like the superior bodies, described as lying inside the thyroid fascia. Our experience has shown, however, that there is here a very important variation, a variation which determines the path of spread of a tumour. They may be situated below the artery, in which case they are usually anterior to the fascia (*Figs.* 203, 204, Position I), or above the artery, when they are often deep to the fascia, being in this case only visible from the posterior surface or after division in the fascia (*Figs.* 203, 204, Position II). This latter position, as far as I know, has not been previously described, although in one of the figures in Dunhill's paper it appears to be depicted in a position behind this fascia. As, however, this variation may lead to a tumour's occupying a most unexpected position, it is, we believe, the most important variation that may occur.

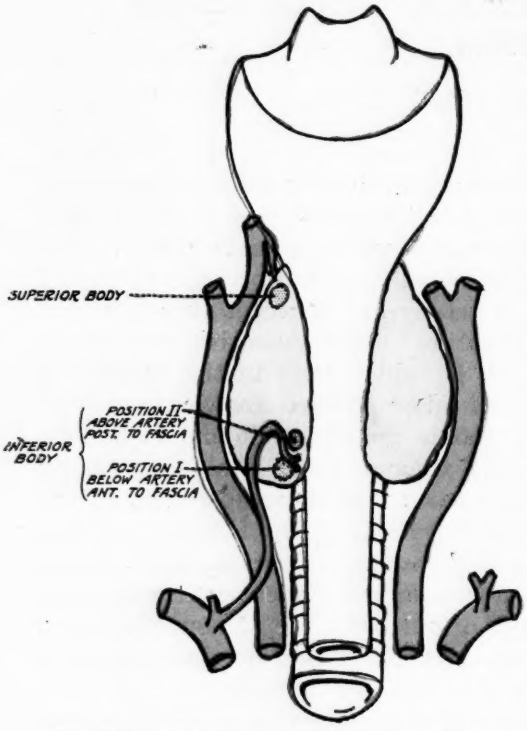

FIG. 203.—Position of parathyroid bodies as seen from behind.

Although the above may be considered as the more or less normal positions, there are other abnormalities which are important to remember. Occasionally one or more parathyroids are situated in the substance of the thyroid gland (*Fig.* 204, Position III). This arrangement, said to be normal in the dog, is rare, but is, however, of surgical importance in that the gland is certain to be removed in a partial thyroidectomy, as in a case reported by Lahey. Also with an expected parathyroid tumour great difficulty may arise if a small adenoma of the thyroid is present; for this may be mistaken for the parathyroid tumour in the substance of the gland, and the true tumour thereby overlooked. Aberrant parathyroids may exist anywhere in the branchial area, and apparently even in

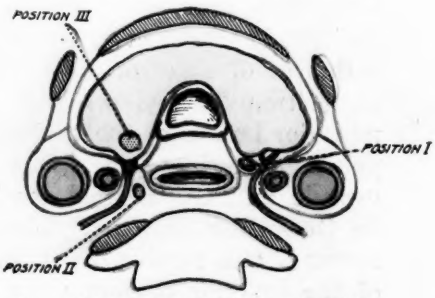

FIG. 204.—Relation of parathyroid bodies to the thyroid fascia.

the substance of the thymus, but I can find no account of a parathyroid tumour being so situated.

Tumours of the parathyroid have been regarded as very rare, and certainly relatively few operations have been performed for their removal. Compere, in 1930, was able to collect only 12 cases in addition to one of his own. It was only in 1907 that Erdheim propounded his view that enlargements of the parathyroid with certain bone disease were an attempt on the part of the organism to compensate for a loss of calcium, and thus were the result rather than a cause of the disease. It was not until 1926 that Mandl, in testing this theory, found that the bone symptoms were increased by parathyroid grafting, and acting on this observation found a tumour behind the left lobe of the thyroid which he removed together with the parathyroids which he had previously grafted into the abdominal wall. The removal of the tumour, which proved to be a parathyroid adenoma, was followed by marked relief.

In this country the recent work of Dr. Hunter has directed considerable attention to these bone changes, and it is very probable that the disease will prove to be much more common than was at one time thought. Since the publication of his first paper he has had four cases in which he has been able to make a positive diagnosis of parathyroid tumour—a diagnosis which I was able to confirm at operation. Although these cases have been so relatively few in number, the operation has brought to light certain difficulties in the technique, and has shown how they may be avoided.

In all cases a light ether anæsthesia was used, and it was realized that a wide exposure was necessary, for since in no case could a tumour be felt it was important to examine not only the normal sites of all the parathyroids, but it was soon realized that the tumour might be situated at some distance from its expected site. A wide collar incision was therefore made, the sterno-mastoids were freed and fully retracted, and the pretracheal muscles divided transversely in one sheet at the level of the isthmus of the gland. By widely dissecting the flaps thus formed upwards and downwards the whole of the thyroid gland is freely exposed from the upper to the lower poles. This gives a much wider exposure than a vertical split in the pretracheal muscles, and if they are carefully sutured afterwards there is no resulting deformity or weakness.

The thyroid fascia is incised, the lateral lobes of the gland are freed and rolled inwards in turn. To accomplish this fully it may be necessary to ligature and divide the middle thyroid vein. By this means a tumour may be at once discovered in the usual site of the parathyroid body, either superior or inferior. In our first case (*see below*) a tumour was thus found in the normal site of the left inferior parathyroid body and was easily removed. In no one of our cases so far has a tumour been situated in the region of the superior parathyroid bodies. Experience of later cases has shown, however, that the real difficulties arose according to the relation of the inferior bodies to the thyroid fascia. If the parathyroid body lies between this structure and the capsule of the thyroid gland (*see Figs.* 203, 204, Position I), it will as it enlarges pass downwards along the inferior thyroid veins and in front of the carotid artery in a manner identical with a retrosternal goitre until it comes

to lie between the sternum and clavicle (*see Fig.* 206, Position I). Hence if no tumour is observed in the usual site, a finger should be passed into the thorax on either side of the trachea. In our third case a little confusion was at first caused by the fact that a small adenoma was present in the left lobe of the thyroid which might have been a tumour in an aberrant parathyroid, but on passing a finger down alongside the trachea a large tumour was at once found in the upper part of the thorax on the left of the trachea, and although it measured about 3 × 1 in. it was easily dislocated and removed, leaving a large cavity immediately behind the sternum exactly like that left after the removal of a retrosternal goitre. Very different is the condition if the parathyroid gland is situated behind the thyroid fascia (*see Figs.* 203, 204, Position II), for when the fascia is opened from the front no sign of the tumour is seen and nothing can be felt in the thorax on examining either side of the trachea.

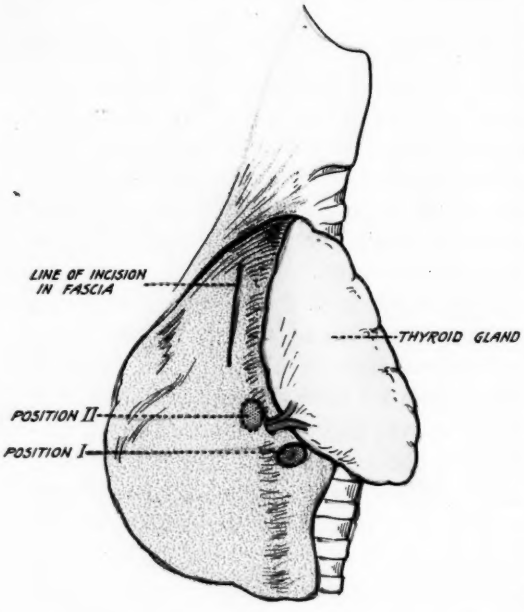

FIG. 205.—Incision in thyroid fascia to expose a deep tumour of the inferior parathyroid body.

In our second case no tumour could be found in the usual situation, but on making a small incision through the fascia above the inferior thyroid artery (*Fig.* 205), a tumour about the size of an almond was immediately found and removed. The importance of this relationship was not, however, fully realized at the time, for the tumour being small had not passed from its normal position.

The position of the tumour in our fourth case brought to light a very important relationship which I believe has not been previously described, and probably explains those cases in which a tumour has not been found at operation. In this case an investigation of the normal sites revealed no tumour, and as a small mass was found in the lower part of the right lobe of the thyroid it was removed in the belief that it might be a parathyroid tumour lying within the thyroid gland. This mistake should not have been made, for Professor Turnbull, who was present at the operation, was convinced, from the colloid appearance of the mass, that it was an adenoma. Sections after the operation confirmed this view, and as Dr. Hunter was certain that a parathyroid tumour was present a second operation was performed five days later. By this time a study of the anatomical relationships had suggested what was later found to be a fact. Therefore when a second investigation had confirmed the view that no tumour was present in the usual sites a small incision was made in the thyroid fascia (*Fig.* 205). A small typical parathyroid tumour was at once found behind the œsophagus and removed, but as a wide space was then revealed a finger was inserted and a large tumour,

as large as a plum, kidney-coloured, was found lying immediately in front of the 2nd and 3rd dorsal vertebra. It was easily dislocated upwards, and its vascular pedicle, which ran from the inferior thyroid artery, was ligatured and the tumour removed. The position of this tumour made it evident that an enlargement of the inferior parathyroid body which is situated behind the fascia passes downwards behind the œsophagus immediately in front of the vertebræ until it comes to lie in the thorax and is quite out of sight (*Fig.* 206, Position II). In this case, as in *Case* 2, the large cavities were drained with a small tube, the muscles were approximated with catgut, and the skin was united with fine sutures. The surgical after-treatment was in no way different from that of a large adenoma of the thyroid, but careful attention had to be given to an estimation of the blood-calcium, and the possibility of the onset of tetany guarded against by the administration of calcium and parathormone. The details of the after-care in this respect have been fully described by Dr. Hunter, and therefore need not be repeated here. The full details of the cases have also been reported by Dr. Hunter (*see* p. 213), and therefore need only be briefly summarized.

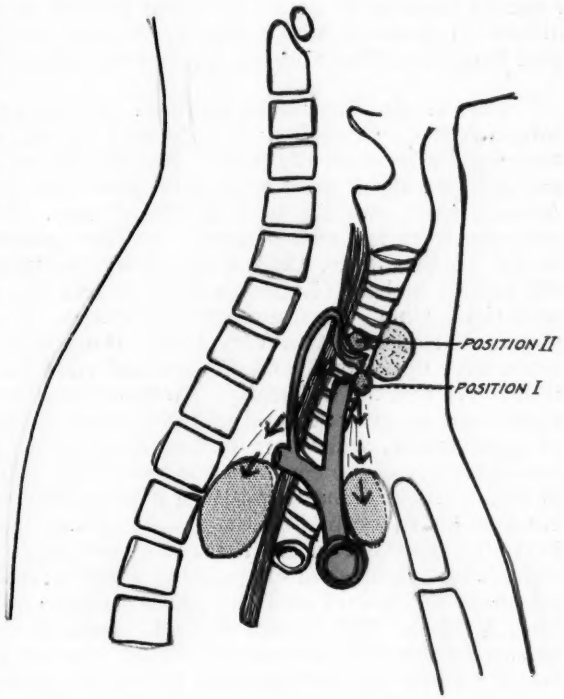

FIG. 206.—Alternative positions of the inferior parathyroid bodies.

CASE REPORTS.

Case 1.—M. M., female, aged 41. For five years pains in joints and limbs. Diagnosed as osteo-arthritis. Five months before admission, X-rayed and diagnosed as osteitis fibrosa. One month before, fracture of neck of left femur. On examination marked hypotonicity of muscles, shortening and eversion of left lower limb, tenderness on pressure over shafts of long bones, tender swelling in lower end of right ulna. X rays showed general osteoporosis and multiple cyst-like areas in right ulna, right tibia, right patella, and phalanges. Increase of serum calcium and a low plasma phosphorus. No tumour felt in neck. Operation on Nov. 29, 1929. Tumour removed from region of left inferior parathyroid. Good recovery and great improvement of all symptoms.

Case 2.—M. R., female, aged 37. Two years pain in knees, hips, heels, and arms. Weakness steadily increasing. For two years unable to get about. Swelling of right lower jaw. Limbs becoming stiff and distorted. Swelling of left forearm and right hand. In many hospitals since. In May, 1930, admitted to the London Hospital. Much deformity. Height 4 ft. 10 in. In bed totally disabled. Hips and knees flexed, cannot move either arm. Great pain in limbs. Bones very tender. All long bones much distorted and bent. Large tumours right lower jaw,

dorsum of right hand, and second metacarpal. General osteoporosis. Heads and necks of both femora absent. All long bones thin and much bent. Calculi in right kidney. Serum calcium increased. No tumour in neck. Operation on July 2, 1930. Small tumour $\frac{1}{4} \times \frac{1}{2}$ in. removed from behind thyroid fascia at site of right inferior parathyroid. Great improvement since operation.

Case 3.—A. F., female, aged 40. During pregnancy twelve years ago difficulty in walking. Easily tired. Child stillborn. Two years ago pain in joints; interfered with walking. Two and a half years, swelling in right tibia, portion removed. Severe pain in right leg since. Swellings developed on left ring-finger, forehead, and chin; varied in size from time to time. In bed owing to pain in joints two years. Some frequency of micturition. Six years ago stone removed from left kidney. Small swelling felt in left lower pole of thyroid. Hard, bony tumours in lower right tibia, skull, left ring-finger. General osteoporosis. Serum calcium increased. Low plasma phosphorus. Albumin in urine; right and left renal calculi. Operation on Aug. 29, 1930. Small adenoma felt in lower left lobe. Large rounded tumour 3 × 1 in. in thorax behind sternum and to left of trachea; easily dislocated upwards and removed. Wound drained and closed. Patient recovered well from operation and has made great improvement since.

Case 4.—B. Y., female, aged 51. At the age of 13 abscess of left hip, probably osteomyelitis. Operation on right arm and left hip at the ages of 14 and 15. Commencing deafness at 16 (1915). Swelling of outer side of right orbit. March, 1926, swelling on right gum with stiff jaw. October, 1926, operation on right jaw. August, 1927, swelling on left side of nose. December, 1927, myelomatous tissue removed from left side of nose. In 1928 general tenderness over bones; swelling in left thigh. June, 1928, deep X-ray treatment. December, 1927, could hardly lift herself in bed. Large swelling in left femur, smaller swellings in right femur and right tibia. Deafness getting worse. Trace of albumin in urine for some years. On examination very thin. Bony swelling on outer aspect of right orbit. Scars over upper end both femora and right humerus. Swelling in middle of right tibia. No marked deformity. General osteoporosis; little bending of right radius. Cystic spaces in upper end of right humerus, upper end of right femur, lower end of right femur, and upper end of right tibia. Thyroid not enlarged; no tumour felt in neck. Urine contains one-twentieth albumin. Small renal calculi. Increase in serum calcium and decrease of plasma-phosphorus. Operation on Nov. 26, 1930. No tumour in normal parathyroid regions. Both superior and left inferior parathyroids identified in their normal positions. Small tumour removed from lower right lobe. Good deal of vomiting after operation. Sections showed tumour to be adenoma of thyroid and the blood calcium was unaltered. Second operation on Dec. 1, 1930. Old wound opened. Incision on right side through thyroid fascia above inferior thyroid artery. Small tumour $\frac{1}{2}$ in. long found behind œsophagus. Large tumour felt low down in thorax immediately on dorsal vertebræ and behind œsophagus; dislocated upwards; found to be the size of a plum and kidney-coloured. Pedicle running from it to inferior thyroid artery ligatured and divided. After this operation there was no more vomiting, the patient rapidly improved, and the serum calcium fell. She has made very great improvement since operation.

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'MADE-TO-ORDER' SPLINTS: THE TECHNIQUE OF CONSTRUCTION AND FIELD OF APPLICATION.

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In the treatment of fractures external supports or splints play a leading rôle. Many, if not most, of the splints still figuring in surgical text-books do not provide adequate and comfortable support for the injured member, and some are frankly preposterous. The ideal splint for any part should be efficient and comfortable to wear, easy to make and to apply; should fit snugly on to a large surface so that it may not move in relation to the patient no matter how he may twist and wriggle; and, lastly, it should be of small cost and easily procurable anywhere at any time. It is obvious that these requirements cannot be met by splints of a fixed shape such as those of metal or wood. These require the skill of a trained surgeon for their application, and only too often are out of gear before the patient has reached the front door.

Suppose that a tailor made suits of clothes to a certain fixed shape, and in order to adapt them to different customers introduced voluminous pads here and there to fill up dead spaces! Even supposing that the pads did not shift, the customers would probably take no great pride in their apparel. Nor would a dentist attain to much popularity if he constructed tooth plates to a standard design. Yet the wooden and metal splints in use in the world of surgery do not and cannot fit, and necessitate the introduction of such substances as cotton-wool, felt, and so on.

It is not the intention of the author to discuss the treatment of fractures, arthritis, and so on, but simply to describe a method of constructing plaster splints. In the first place consideration will be given to certain principles which apply in general, and in the first section reference will be made to the materials used and certain points of importance in the manipulation of plaster-of-Paris. Later the construction of certain splints will be described. These are to be regarded as samples only. The breadth of the field of usefulness of the method is proportional to the amount of ingenuity possessed by the surgeon.

GENERAL CONSIDERATIONS.

The best form of fixation for the fragments of a broken bone would be a closely-fitting ferrule, such as is used to unite the segments of a fishing rod, but this is out of the question as the bones are surrounded by soft parts. It is, however, absurd to introduce *more* soft and yielding material between skin and splint, and in general it may be stated that the more closely the splint approaches the bone fragments to be supported the better will be the fixation. Therefore, it is desirable that the apparatus should fit directly and snugly on

to the skin of the part. Now circular plasters could be made in this way, but for many reasons which need not be discussed these are unsatisfactory and often dangerous. It will be seen later that most of the splints described are more or less semi-cylindrical or crescentic in section. Thus ample provision is made to permit of swelling of traumatized tissues and ensure against constriction of the part. It may be stated dogmatically that a well-fitting plaster support never causes the least damage to healthy skin, either on account of its chemical constitution or its physical characteristics; and, conversely, that sores are always the result of errors in technique.

The snug fit, in addition to ensuring the maximum of efficiency, carries with it other advantages. In many instances cotton-wool and similar substances may be dispensed with entirely, and in some (e.g., the humeral and clavicular supports) no bandages are required. Removal is easy and re-application is almost fool-proof. Thus when the time comes for voluntary movement, massage, and so on, the management of the splint may be left safely to any intelligent individual, with consequent great saving in time to the surgeon. Inspection of the uncovered portion of the limb is easy without removal of the plaster at all.

Materials Used.—

Plaster-of-Paris.—It is not necessary to pay high prices for special grades. Any plaster which will set satisfactorily in from ten to fifteen minutes will do.

Scrim, or Hessian.—This is made in various weights. It is better to use scrim with a wide mesh, as this adapts itself well to surfaces of irregular contour and is easily penetrated by the plaster cream. 'Eight-ounce scrim' is the most satisfactory and may be obtained at any decorators. As a fabric it is much cheaper and far more serviceable than the ordinarily used leno.

Gauze, in rolls one yard wide.

Webbing Strips.—These are obtainable in various widths and should be stout and inextensible. The most useful widths are one inch and two inches.

Buckles with sharply pointed prongs in sizes to fit the strips to be used.

In addition to the above all sorts of odds and ends are at times incorporated in the plasters at the whim of the surgeon. It is the practice of the author to carry in his car a supply of the above-mentioned materials, with the result that at any time or place he can manufacture a really efficient splint. The saving in time and trouble which results from this simple provision is considerable.

Garb of the Operator.—It is well to prepare for the worst. The surgeon should wear a gown, canvas leg covers like waders, and rubber gloves. The skilled manipulator of plaster does not, however, make much mess.

THE MAKING OF PLASTER SPLINTS.

The method to be described is very easy, but success depends on attention to detail, and in particular it is important to have everything in readiness before mixing the plaster cream. First of all the materials to be used must be prepared. A strip of gauze is cut measuring twice the width of the area to be covered and as a rule at least from six to twelve inches longer. There is no need to shape the gauze. Too small a piece will cause trouble later,

whilst excess is easily cut away when the time comes. Strips of scrim roughly corresponding to the shape of the proposed splint, but always a good deal smaller in all directions, are then cut out. For very small plasters about three or four will suffice; for plaster beds about a dozen or more should be prepared. Small scraps of scrim may be used to insert where extra thickness is necessary. Strips of webbing of the appropriate length should be cut. Buckles are affixed when the splint is removed for trimming. If it is proposed to use wires, metal strips, and so on, these must be to hand and shaped appropriately. When all the materials to be used are ready attention is transferred to the patient.

Infinite pains must be taken to place the part in question in the required position, and here gentleness and patience avail more than anything else. It is useless to make a support on a limb in the wrong attitude, for once this is done there is no means of altering the state of affairs. The surface on which the slab is to be laid is arranged so as to face upwards if possible, and sand-bags or other objects are placed where necessary so that the part is supported firmly in the correct alinement. The preliminary posing of the part is the most important detail in the manufacture of these splints, and no amount of skill in the carrying out of other manipulations will compensate for shortcomings here. An anæsthetic may be given to attain the desired result, but this is not necessary as a rule.

From this point onwards until the completion of the process there should not be the slightest disturbance of the injured part. The advantages of this method when compared with others, which frequently enough are attended by movement, pain, and consequent spasm, should be obvious.

When the surgeon is satisfied with the position of the patient the piece of gauze is laid over the surface in question with its edges projecting all round. It is then time to mix the plaster cream. A bowl of convenient size is taken and the required amount of water with the chill off is poured in. Plaster is then dusted on to the surface of the water so that it is wet as it falls in. Enough is added to produce a cream which will not easily run out of the meshes of the scrim, but which is thin enough to penetrate thoroughly the strands of the fabric. The bowl of cream and other materials are then placed a few inches only from the seat of operations. This is important, as thereby much time is saved and the amount of plaster dropped in transit from bowl to splint is minimized and localized to a small area. A little cream is next smeared on the gauze where it is in contact with the skin to ensure that it will be properly incorporated in the finished article. A strip of scrim is taken, laid dry on the appropriate area, and immediately smeared over with plaster cream, care being taken to fill all the interstices of the fabric to the exclusion of air. Other strips are then added in a similar way until the required thickness is attained. The reader will remember that the strips were cut smaller than the area to be covered. They are placed so that whilst they overlap along the middle line of the splint, alternate layers only reach to one or other edge. Thus thick clumsy margins are avoided and, without sacrificing strength, weight is cut down. Reference to *Fig.* 207 will make this arrangement clear. Any ragged tags or corners are cut away with scissors as each layer is placed in position. If any webbing bands are to be incorporated,

these are laid at the appropriate positions between two of the layers of scrim and are thus firmly welded into the plaster.

When the requisite thickness is attained the margins of the gauze projecting beyond the splint edges are turned back over the surface of the latter and cemented down with a little of the cream. By a process of wiping the plaster away from the margins into the body of the structure a neat thin edge bound by the reflected gauze layer is obtained. The gauze must be cut in order to permit of this turning back where webbing strips emerge. As the setting process begins the surface of the plaster is smoothed over by the gloved hand, which is frequently rinsed in water. When set the plaster structure is removed for inspection and the patient's skin may be cleaned. The splint is then re-applied and fixed in position by bandages or webbing bands as the case may be. A single layer of very thin material such as silk or gauze may be worn between skin and plaster.

FIG. 207.—A diagrammatic representation of a cross-section through a plaster splint, to show the following points. The plaster extends about half-way round the circumference of the limb. Strips of scrim are so disposed that at the centre of the splint there are many layers, at the edges one. Thus a bevelled or crescentic effect making for neatness and lightness combined with strength is obtained. The interrupted line represents the enveloping layer of gauze which serves to bind the edges as well as to hide the coarse meshes of the scrim.

All of the splints to be described are made as outlined above, but there are certain other points to which attention must be drawn. When the area on which the slab is to be constructed is hairy it is wise to smooth down the hair with a thin smear of oil or vaseline. Shaving is unnecessary. If the splint is removed as soon as it has set, such hairs as have become caught in its surface are easily freed without causing pain. When making plaster beds and splints such as those described for the treatment of fractures of the clavicle and humerus precautions are taken so that the skin over prominent bony points may be guarded from trauma. Before applying the gauze a disc of cotton-wool, measuring 2 or 3 in. in diameter and about $\frac{3}{8}$ in. in thickness at its centre and fading away to the periphery, is prepared and placed directly on the skin area in question, after wetting the latter with water so that slipping of the wool during subsequent manipulations is hindered. The wool is removed from the finished plaster and thus a shallow depression in the surface is provided for the reception of the bony prominence. Should the splint press upon or rub the skin at any point, causing pain, the tender spot is marked with ink, the splint is re-applied and on removal the offending part of its surface is seen to be plainly marked. The plaster is then scraped away so that contact with the skin is eliminated. The surgeon should always aim at providing a shallow, shelving trough rather than a sharply defined hole for the reception of prominent points.

When there is a wound or ulcer in the region of the part to be splinted matters may usually be arranged so that the apparatus is made on the healthy aspect of the limb. Dressing of the wound is thus easy. If, however, it is necessary to make the splint on the affected aspect of the part in question, a dressing should be fixed in position over the wound or ulcer and then

covered with a layer of oiled silk or other waterproof material. The splint is then constructed over all, and when finished contains a recess for the accommodation of the dressing. It is not necessary to bandage the dressing as it is held firmly in position by the applied splint.

Sometimes it is desirable to coat over the plaster apparatus with shellac dissolved in methylated spirits. Several coats may be applied with an ordinary varnish brush. The resulting surface is hard, smooth, durable, and waterproof, and may thus be washed. Plaster beds and other splints which are designed to serve for more than a short period are, as a rule, treated in this way.

In order that the splint may be strong and yet light and neat in appearance, the following points should be observed. Tubular structures are immensely strong, and to a less degree so are semi-cylindrical forms. Hence the plaster should be constructed so as to approach the latter form wherever possible. When the curve is small or absent the segment in question must be made much thicker to compensate for the inevitable loss of strength. Thus in a plaster bed the interscapular region is flattish and must be made very thick. Weight is reduced and neatness in appearance attained by bevelling so that the splint diminishes in thickness from the centre in all directions to the margins. It is never necessary to incorporate metal in order to augment strength.

INDIVIDUAL SPLINTS.

In this section it is proposed to deal briefly with some of the more important points arising in connection with the construction of some useful splints. Surgeons who have the necessary ingenuity and the will to do so will have no difficulty in designing and constructing apparatus to meet almost every conceivable contingency.

Plaster Beds (*Figs.* 208–210).—The patient lies prone with a pillow under the pelvis and upper chest, and a block supporting the forehead. The arms are abducted, forming with the body an angle of not more than 20°. Bony prominences are cared for as outlined above. It is wise also to fill up deep grooves, such as that over the spines of the lumbar vertebræ between well-developed erector spinæ muscles, with wool, in order to avoid prominent ridges on the bed surface. The bed is shaped like the posterior half of a waistcoat, but extends well on to the buttocks and reaches always to the base of the neck, and, if the lesion is above the 6th dorsal vertebra, to the occiput or further. Laterally the edges reach to the mid-axillary line. It is necessary to make the apparatus especially thick in the scapular region to guard against breaking. Often a large 'hump' of scrim and plaster is built on the dorsal aspect in the lower lumbar area. This raises the lower edge from the bed and facilitates the use of the bed-pan. It is better to make the plaster bed too heavy rather than too light. For an adult about 18 or 20 lb. of plaster should be used, but the amount varies of course with the bulk of the patient. The surface is usually coated with shellac varnish. A well-made plaster bed properly used will last for years and provides a very efficient and comfortable support for the trunk. The cost of materials used is about five or six shillings.

A very satisfactory apparatus (*Figs.* 211, 212) for the treatment of arthritis of the hip and some fractures of the femur (where extension is not needed), and for supporting the limb after operations such as grafting an

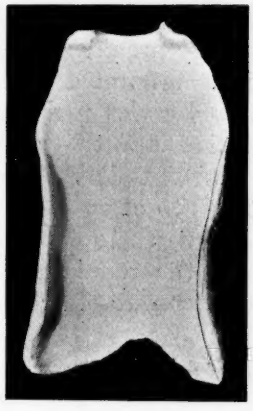


FIG. 208–210.—A plaster bed for use in the treatment of injuries and diseases of the spine. Note the pronounced lateral projections in the pelvic, thoracic, and neck regions; and the hump, which permits of see-sawing with but little effort on the part of the nurse. *Fig.* 210 shows the buttocks raised to facilitate the use of a bed-pan, a support having been removed from the shoulder region.

un-united fracture of the femur, may be made by extending a plaster bed down to and including the foot. Similarly, an extension may be provided to support the arm in a position of wide abduction at the shoulder. If such splints are made prior to operation, a dummy dressing should be placed in

FIG. 211, 212.—A plaster bed with leg extension. This splint was made prior to operation for fixation of the hip-joint. A dummy dressing was applied over the site of operation in order that there should be a recess in the plaster surface for the accommodation of the post-operative dressing. Fixation is very efficient and transportation easy.

position on the limb in order to provide a recess for the accommodation of the post-operative dressing.

Apparatus Used in the Treatment of Fracture of the Clavicle (*Figs.* 213–215).—Two plaster slabs are made, one on the sound shoulder, the other on the elbow region of the affected limb. The first is to carry the weight of the injured limb and apparatus and is made on the patient in the upright position.

It is oval is shape, reaching to the clavicle in front and well on to the back behind. A strip of webbing with a buckle at each end is incorporated. The second slab is moulded over the elbow region of the injured limb whilst the patient lies supine with his injured shoulder thrust cranially and his hand placed well over his sound shoulder. A flange about two inches wide fits on to the thorax. The bony points round the elbow are provided for as outlined in the previous section. A webbing band is incorporated to link up with the weight-carrying slab. The provision of two buckles makes adjustment easy, and the limb carrying the outer fragment is supported so that the shoulder is a good deal higher than that on the uninjured side. The elbow region is firmly fixed, and the weight of the limb tends to carry the shoulder backwards and outwards with this fixed point as a centre of rotation. This movement almost always brings the fragments into the required position. The apparatus, when properly applied, can scarcely get out of adjustment,

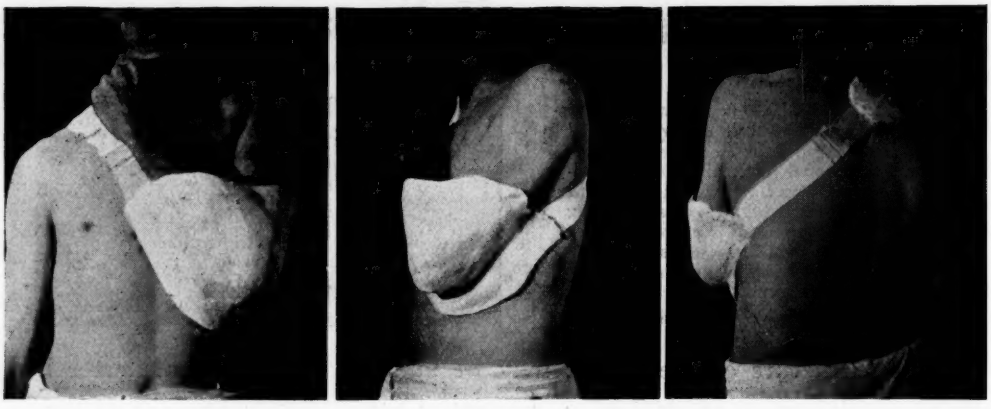


FIG. 213–215.—Apparatus for the treatment of fracture of the clavicle. Note the weight-bearing slab on the sound shoulder, which carries the weight of the elbow slab and arm of the affected side. The affected shoulder is held higher than normal. The elbow is fixed. The weight of the limb carries the shoulder backwards and outwards along an arc of a circle drawn with the elbow as its centre. The shoulder slab is made in the upright, the elbow slab in the recumbent, position.

as do most appliances used to treat fracture of the clavicle. The shoulder slab, in addition to providing a very comfortable bearing surface, makes rotation of the apparatus round the trunk practically impossible. This might occur if the lower slab were supported by a fabric band only, and in addition the latter would tend to cut into the skin and cause pain. Should the slabs cause trouble over the clavicle or bony points at the elbow, the plaster should be scraped away as described above. When it is necessary to remove the apparatus the patient should lie supine so as not to disturb the relationship of the fragments. The elbow- and shoulder-joints may then be exercised. The hand and wrist movements are not hampered in any way by this apparatus.

Apparatus for Use in the Treatment of Fracture of the Shaft of the Humerus (*Figs.* 216–218).—Note: The brachial portion of this apparatus is a modification of a splint originally designed by Mr. Fay Maclure, of Melbourne.

The position of rest for the upper limb is that shown in *Fig.* 216. When

a normal limb is slung in this way the elbow is well away from the side. Obviously it should be held in a similar position when the humerus is fractured. The elbow is bent at about a right angle and the wrist is supported by a sling or bandage from the neck. If a patient with a fracture of the shaft of the humerus is given morphia and left sitting for half an hour with his arm so supported, almost always muscular spasm disappears and the limb

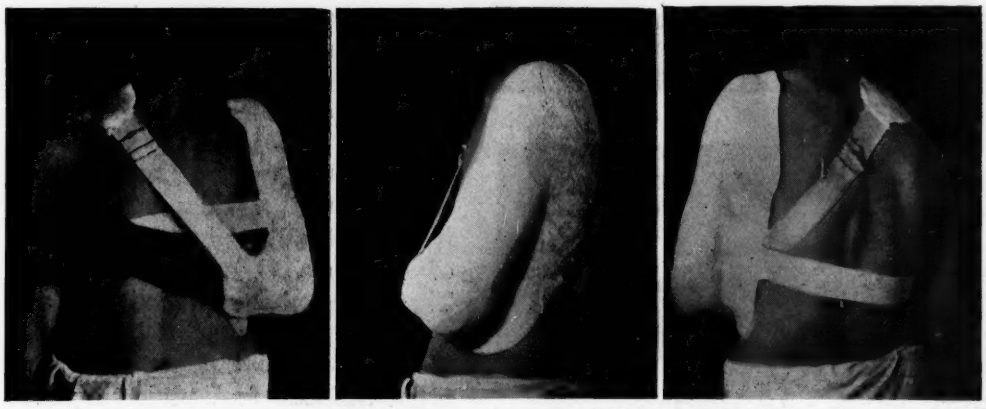


FIG. 216–218.—Apparatus for the treatment of fracture of the humerus. Note the weight-bearing slab and the brachial splint which consists of a postero-lateral gutter supported by a flange or buttress fitting on to the thorax. Both plasters are made on the patient in the sitting position, the wrist being slung from the neck in the position shown. The sling is omitted for the sake of clarity, but is of course worn with the apparatus. The elbow is well away from the side. The webbing bands pass right through the slabs.

takes on a normal appearance. It then remains to build a splint which will maintain the position. The splint used is a postero-lateral gutter supported above, posteriorly, and below by a buttress or flange fitting on to the thoracic wall. It is held in position by two webbing bands, one passing round the thorax, the other linking up with a weight-carrying slab similar to that used in the treatment of fracture of the clavicle. Both slabs are made on the patient in the sitting position. There is no constriction of the limb at any point. Immobilization is excellent. Jolting and jarring fail to move the apparatus relatively to the patient, and direct force applied to the slab is transmitted to the trunk without disturbing the injured segment of the limb. Inspection of the limb is easy. To remove the apparatus it is necessary to undo two buckles only. This should only be done whilst the patient is upright with the wrist supported by a sling from the neck.

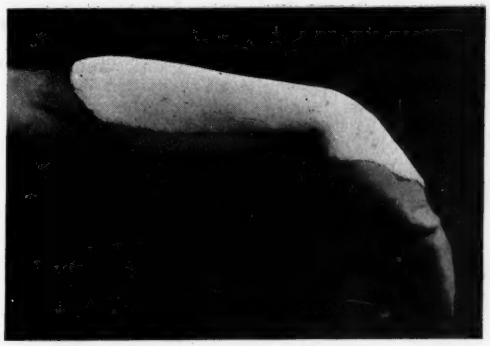


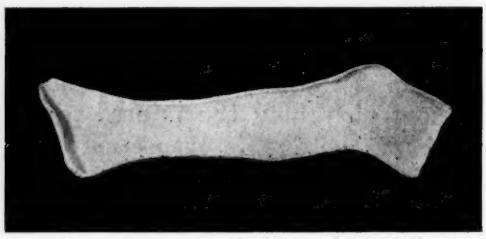
FIG. 219.—Splint moulded to support a wrist in flexion. A cock-up or any other form could be easily constructed.

Injuries in the Region of the Wrist (*Fig.* 219).—The arm and hand are supported on a table in the desired position, and a slab of the requisite length

is moulded on the upper aspect. In making very small slabs a gauze bandage is sometimes used instead of strips of scrim. Well-made slabs are more comfortable and efficient than wooden or metal splints in the treatment of injuries and diseases about the wrist-joint. The dimensions and shape of the slab and the attitude of the limb to be treated vary with circumstances. As with other splints of this type, removal is easy and re-application practically foolproof.

FIGS. 220–222.—A posterior splint for the leg. *Fig.* 222 pictures the position in which the limb is supported during construction of the plaster slab, but the support shown would be inadequate in practice. *Fig.* 221 gives another view, and *Fig.* 220 shows the splint alone. Note the accurate fit, the thin edges, the flexion at the knee. This splint is very strong on account of its shape, particularly where the foot and leg pieces merge. It is 'semi-cylindrical' throughout its length.

Splints for the Lower Limbs (*Figs.* 220–224).—Plaster slabs are particularly useful in the treatment of fractures of the Pott's type. They may be moulded on any aspect of the limb. A back splint is made with the patient lying prone and the foot projecting over the end of the couch or large sand-bag. Side splints are very efficient, and the author frequently uses these, more particularly when inversion of the foot is desired or when there is a wound on the medial or lateral aspect of the limb. The patient lies on one or other side with the limb suitably supported on sand-bags. When both bones of the leg are fractured it may be necessary to control the fracture for a week or so by some method of extension prior to the application of a slab. Recently Mr. E. T. Cato has brought to the author's notice a useful device. With the



FIGS. 223, 224.—A lateral splint for the leg. *Fig.* 223 shows the position in which the limb is supported during construction of the apparatus. The support shown is, of course, inadequate. In *Fig.* 224 the splint is seen alone. Again the semi-cylindrical form is preserved.

patient lying prone traction is exerted on the foot through the medium of a bandage passed round the foot and ankle. A posterior slab is laid on as usual, extending well above the knee, which is slightly flexed. When set, the protruding ends of the bandage are cut away. There appears to be very little tendency for overlapping of the fragments to recur when this method is used.

SUMMARY.

It is pointed out that many of the splints used to treat fractures are not well fitted for the purpose. A plea is made for the recognition of the many advantages attending the use of snugly-fitting plaster-of-Paris slabs. Whilst these are very efficient and comfortable for the patient to wear they also save the surgeon much time and trouble. The author's methods are briefly described.

The splints are made of plaster-of-Paris reinforced by strips of 'eight-ounce scrim', or hessian, and bound by a layer of gauze, and are moulded directly on the skin surface of the patient. Thus neatly shaped, thin-edged, light, strong, and accurately-fitting supports free from clumsy wrinkles are obtained, which are very easily managed. Wherever possible the splints approach in section the semi-cylindrical shape, which makes for strength and efficient support whilst avoiding any danger of constriction of the part.

Careful placing of the injured part in the best possible position is of first importance, and this is done deliberately before commencing operations. The part is firmly supported on sand-bags, and during subsequent manœuvres is not disturbed in any way. In certain instances webbing bands provided with buckles are built into the splints and bandages are dispensed with. Cotton-wool is used only on the limb surface which is *not* covered by the plaster, to permit of swelling of traumatized tissues when bandages are used. A single layer of very thin material such as silk or gauze may be worn between skin and plaster.

Methods of dealing with various difficulties are discussed. Certain individual splints are described, but it is pointed out that these are only examples of what may be done with the method. The surgeon who masters the technique and has sufficient ingenuity will be able to devise for himself splints of infinite variety. If he takes the simple precaution of having the materials always at hand, he will be prepared to produce an efficient apparatus at any time. Success depends upon attention to detail, and practice. The more the surgeon uses the method, the more useful will he find it.

It is not intended to imply that there is never any need for other forms of apparatus, nor that the splints are more than an aid to the surgeon in the treatment of fractures, arthritis, and so on.

The author wishes to convey his thanks to numerous colleagues from whom he has received useful hints, to patients who have taught him much, to many house surgeons who have cheerfully helped him in the production of photographs, and lastly to Mr. Fay Maclure who first brought the idea of plaster slabs before him and who has since then never failed to take a kindly and helpful interest in the development of the present methods.

REGENERATION OF THE INTERNAL SEMILUNAR CARTILAGE AFTER OPERATION.

By A. GIBSON, Winnipeg.

In an excellent monograph on internal derangement of the knee-joint[1] there is related the history of a case in which both semilunar cartilages were removed 'elsewhere', the internal on Aug. 8, 1921, the external on April 5, 1922, yet "on full exposure it was seen that both semilunar cartilages were present. The internal was normal. . . . The fact that this patient had undergone operations by the 'classical' routes upon both cartilages and a more complete exposure showed them both to be present is particularly instructive. The finding of a cartilage alleged to have been removed has probably befallen most of us, and this fact is a strong argument in favour of a complete exposure." Not necessarily!

On Oct. 8, 1928, J. W. O., machinist, came under my care. On May 30, 1928, he was pulling down a big wrench with all his weight. His right knee came violently against a plate under his bench. From that time onward he complained of something slipping in the right knee-joint. On Aug. 10, 1928, he was operated on 'elsewhere' and had not been back at work since. On the morning of Oct. 8 the joint seemed to lock.

On examination an oblique scar was present on the medial side of the right knee. There was considerable swelling of soft parts and considerable heat. Extension was possible to an angle of about 165°. Flexion was possible to about 90°. Examination by means of the X rays showed no loose body in the joint. There was atrophy of the patella and of the adjoining part of the femur.

On Oct. 23, 1928, a 'complete exposure' was made by parapatellar incision. The internal semilunar cartilage was in position; its posterior extremity was much thickened. The synovial membrane of the joint was hyperæmic. A considerable part of the internal semilunar cartilage was removed and was sent for microscopic examination. The report was as follows: "Specimen consists of dense fibrous tissue only—no cartilage cells." *Fig.* 225 shows a normal human meniscus, and *Fig.* 226 that of this patient. With this finding in mind it was decided to submit the matter to experiment.

On May 8, 1929, two dogs were operated on; the knee-joint was opened and part of the internal semilunar cartilage removed by the 'classical' route. The dogs were turned loose on a farm for the summer and showed no disability. On Oct. 4, 1929, one of them was brought in and sacrificed, and both knee-joints were examined. There was apparently complete restitution of the internal semilunar over the area of operation (*Figs.* 227, 228). Microscopic

examination showed the specimen to consist of dense fibrous tissue only with no cartilage cells.*

Mandl[2] has described three cases in which a 'delicate structure' replaced

FIG. 225.—Normal human meniscus. (× 400.)

FIG. 226.—Meniscus of J. W. O. (× 250.)

* This specimen was shown at the Orthopædic Section, British Medical Association, Winnipeg, in August, 1930.

the excised semilunar cartilage. In the patient and the dog mentioned above, the replacement was in no way delicate. It was if anything superior to the original.

FIG. 227.—Dog. Normal meniscus. (× 400.)

FIG. 228.—Dog. Regenerated meniscus. (× 400.)

Lukjanov and Pokrovski[3] operated on 37 dogs, of which 12 died post-operatively (!). They found that " removal of the menisci, partial or complete, has resulted in regeneration of the cartilage. These differ from the normal

ones neither in form nor consistency; they are only less glossy and movable. The newly formed semilunar cartilages are functionally and statically of equal value with the ones removed."

It would seem, therefore, that we have consistently underestimated the restorative power of the body in assuming that a semilunar cartilage when excised is excised for good. Our patients generally ask us what degree of function they may expect after the operation of meniscotomy, to which we generally reply with confidence that full function may be looked for. The experimental findings mentioned above may furnish an anatomical as well as an empirical basis for the faith that is in us.

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[3] LUKJANOV and POKROVSKI, *Jour. Sovremmenoi Chir.*, 1929, iv., 946 (abst. in *Jour. Bone and Joint Surg.*, 1930, Oct., 984).

EXPOSURE OF THE KNEE-JOINT.

By H. B. DEVINE, Melbourne.

The indications for operation on the knee-joint may be divided for practical purposes into two classes, according to whether a definite diagnosis may or may not be made :—

1. First, those conditions where the lesion is localized and where it is possible to make a definite diagnosis, and the surgeon is reasonably certain that if he makes an exposure over the affected part of the joint, he will be able to deal with the lesion. Such, for instance, is internal derangement of either of the menisci. Here, if the classical syndrome is present, there is very little possibility of a mistake in diagnosis and that an exploration will be unnecessary. The best surgery in this case is to disturb the main part of the joint as little as possible, for we know that the knee-joint has a small margin of error, both as regards operative trauma and sepsis.

2. The second class includes all those conditions of the joint which give a syndrome like an internal derangement of a meniscus and which are mistaken for it—for example, loose bodies or nipped hypertrophic synovial fringes. In these patients a normal cartilage is often removed in the belief that it is diseased, because the surgeon is satisfied, on account of the inadequate exploration possible, that there is no other lesion. Similarly, if a loose body or a nipped synovial fringe is found, it is impossible to make sure that there are not others. A small injury to the crucial ligaments sometimes cannot be recognized through the limited exposure. For these reasons, and others that could be mentioned, the symptoms and disability of the patient recur.

It is surgically more correct in these cases to treat the joint as one would the abdomen in indefinite abdominal conditions—that is, employ an operation which approaches in a simple way the middle of the joint, which brings the whole joint under vision without an unnecessarily big opening, which can be closed without using non-absorbable material, and which heals quickly enough to allow early movement.

There are three recognized methods of exposing the knee-joint : Kocher's operation,[1] Timbrell Fisher's,[2] and the operation (after Hamilton Russell[3] and Sir Robert Jones[4]) in which the patellar tendon, the patella, and quadriceps tendon are split longitudinally. In all these operations the joint is approached through longitudinal incisions, which must divide joint structures extensively in order to give the necessary exposure of the transverse joint surface of the tibia. Anyone who has seen the beautiful exposure of the joint that is obtained when operating on a fractured patella will appreciate that the natural approach to the knee-joint should be through a transverse incision.

The operation described below is based on an approach through a transverse incision by means of which the knee-joint may be explored and operated on in a manner comparable with explorations of the abdominal cavity—that is, by its means, perfect exposure, complete exploration, certain control of bleeding, and physiological closure may be obtained.

TECHNIQUE OF THE OPERATION.

The steps of the operation are as follows :—

1. A curved incision, the middle of which is about half an inch below the lower margin of the patella, is made (*Fig.* 229). A flap of skin and fat is turned up and protected in the usual way.

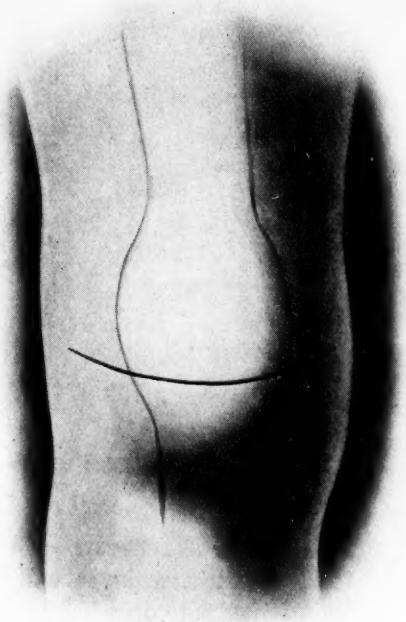

FIG. 229.—Incision for exposure of the knee-joint.

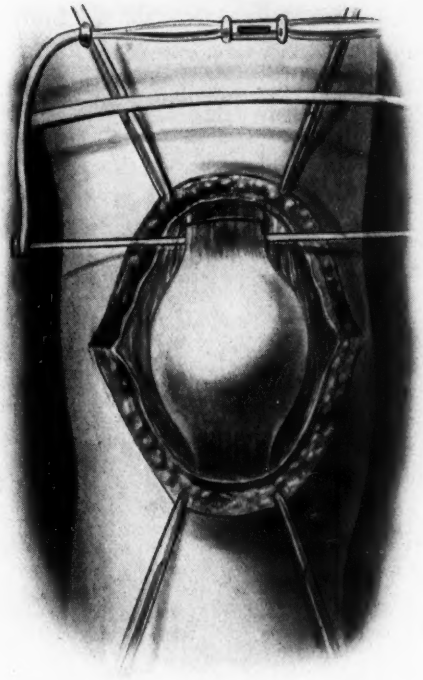

FIG. 230.—Beginning of the longitudinal (coronal) saw-cut through the patella.

2. With a butcher's saw, starting in the quadriceps tendon about half an inch above the upper margin of the patella (*Fig.* 230), a cut is made in a direction which slopes backwards through the tendon of the quadriceps, the patella, and the patellar ligament, coming out of the latter on the posterior surface half an inch below the lower margin of the patella. The object is to separate the anterior half of the patella from the posterior portion without disturbing the cartilaginous surface, and to commence and complete the saw-cut so as to leave attached to each plane of the patella a strong piece of tendon by means of which the patellar segments subsequently may be united firmly with catgut sutures.

3. The assistant bends the knee; the patellar fragments separate and the lateral expansions of the joint stretch tightly. The surgeon now puts a small hook under the lower margin of the upper fragment and turns its cartilaginous surface over (*Fig.* 231), and as the knee continues to bend, he applies his knife in the direction of the vessels to the tightly stretched lateral expansions till he has exposed the joint sufficiently for his purpose. As a rule there is little bleeding.

4. Manipulations may now be carried out with very little instrumentation and certainly without any handling, because the joint is so accessible. All bleeding is stopped and the joint is left quite dry.

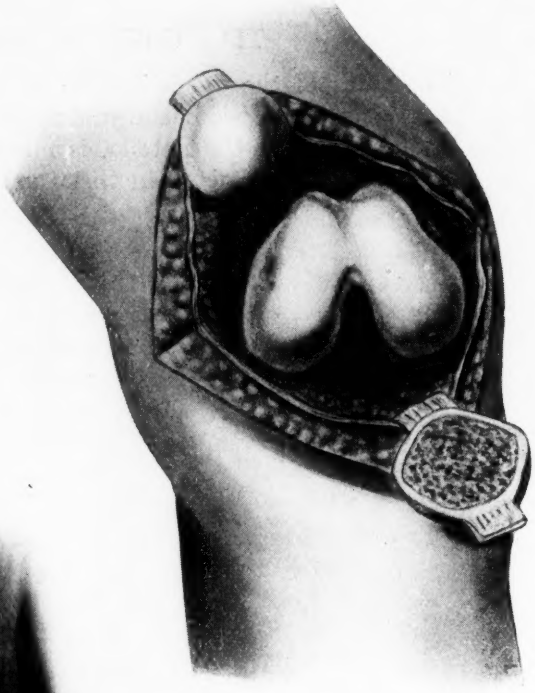

FIG. 231.—Full exposure of the knee-joint.

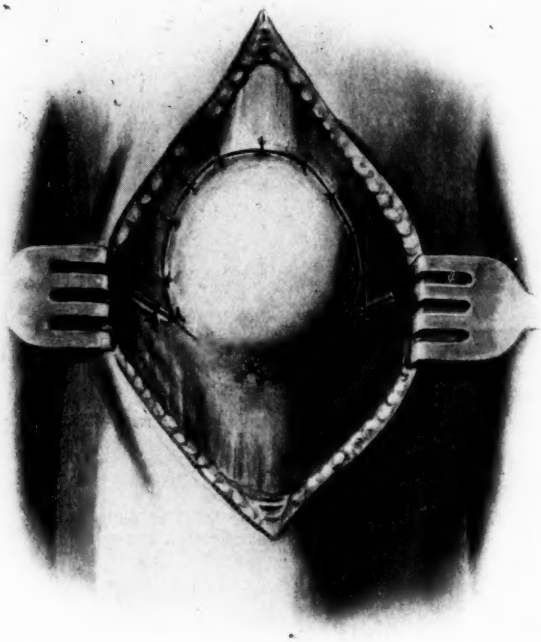

FIG. 232.—The patella sutured back into position.

5. The assistant now extends the leg, when it will be found that the opening in the joint closes and the sliced patellar fragments lie nicely in apposition. The fragments are then fixed together by suture, with catgut, of the obliquely sliced patella and quadriceps tendon. The synovial membrane and the quadriceps expansion are closed separately (*Fig.* 232).

Since it is not possible to guard against the occasional unexpected reactionary hæmorrhage, which has dangerous potentialities as a cause of post-operative complications, the use of a tourniquet in knee-joint operations should be regarded as dangerous. In the operation described there is no

need for a tourniquet, for not only is bleeding avoided by operating through a comparatively bloodless area, but since it is possible to see what is happening, bleeding may be easily and certainly controlled by ordinary methods.

The large patellar raw surfaces make for a firm and early union, and in ten days it is difficult, with an X-ray, to see the line of contact (*Fig.* 233).

FIG. 233. — Skiagram showing union of patellar segments ten days after operation.

The exposure makes the joint so accessible that manipulations can be carried out with the greatest precision and gentleness.

It is our experience that it is an operation which leaves nothing to chance; and that, if the surgeon utilizes his skill and cunning, he can leave a joint which heals rapidly with little reaction and no adhesions, and allows early function.

We could quote many instances where in doubtful cases of internal derangement we were tempted to do the limited operation, where we should have hesitated to do the more formidable recognized exploratory operations, and where the operation described disclosed unexpected conditions such as a hidden loose body, a strong string-like adhesion associated with the crucial ligaments, unsuspected early tubercle, partial injuries to the attachments of the crucial ligaments, osteo-arthritic manifestations, and other lesions.

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CHOLECYSTITIS GLANDULARIS PROLIFERANS (CYSTICA).

By E. S. J. KING,
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Cholecystitis glandularis is a circumscribed or diffuse thickening of the wall of a chronically inflamed gall-bladder, characterized by excessive proliferation of and invasion of the wall by epithelium, forming crypts, with dilatation of some of these crypts to form cysts.

This condition has been described many times under several names: adenoma,[8, 30] polyp,[28] cystadenoma,[15] adenomatous polyp,[31] papilloma,[9, 21] fibro-adenoma,[10] fibromyoma,[32] carcinoma,[27] cholesterol cyst,[8, 13, 24] precancerous proliferation,[33] and sometimes has been discussed without being regarded as of any special significance.[12]

The routine examination of 400 gall-bladders removed at operation for cholecystitis or cholelithiasis demonstrated 38 organs (9·5 per cent) showing this type of change. Twenty-five well-marked specimens were chosen to form the basis of this paper. Since they possessed certain characteristics in common, which distinguished them from other conditions, they were grouped together.

Terminology.—A study of the various conditions which resemble those referred to here and which are described in the literature shows that they all occur in association with chronic cholecystitis and manifest morphological similarities.

In 1922 Bodnár[5] described a diffuse form—the most characteristic feature being the presence of cysts of various sizes in the wall of the gall-bladder, and he styled the condition 'cholecystitis cystica' in analogy with cystitis cystica and ureteritis cystica. Although this is an excellent term and might be used to apply to many of the examples, it does not embrace the cases where cystic change is not predominant.

The term 'cholecystitis epithelialis heterotopica' suggested itself, but this covers too many cases, since a large number of chronically inflamed gall-bladders show heterotopic proliferation of epithelium but not the characteristic macroscopic appearances. This term, also, is too unwieldy for ordinary use. We would suggest that a better name is 'cholecystitis glandularis proliferans'. Though an etymological hybrid might be considered undesirable, the term is suitable from every point of view except that of the classicist, but we have innumerable examples in medical literature as precedents for such a transgression.

GENERAL CHARACTERISTICS.

As stated, cholecystitis glandularis presents itself as a thickening in some portion or portions of the wall of the gall-bladder, this thickening being

honeycombed by epithelium-lined ducts. It may occur in any part, but we have observed it most frequently and characteristically in the fundus of the organ. In the cases examined there has been evidence of chronic cholecystitis in the wall away from as well as in the specially thickened tissue. This special tissue sometimes is demarcated abruptly from the surrounding gall-bladder wall, but in other cases it merges gradually into the neighbouring parts.

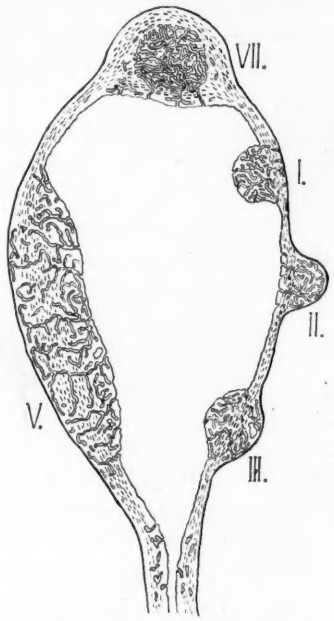

FIG. 234.—Diagram illustrating some of the forms of cholecystitis glandularis which have been encountered. For fuller details *see Fig.* 235.

Rarely the tissue may have an apparent capsule. Macroscopic cysts are not an invariable feature of the group under consideration.

The Macroscopic Appearance.—Several appearances, all merging from one to another, may be observed.

The thickening of the wall may project into the cavity of the gall-bladder (*Figs.* 234 I, 235 I). This

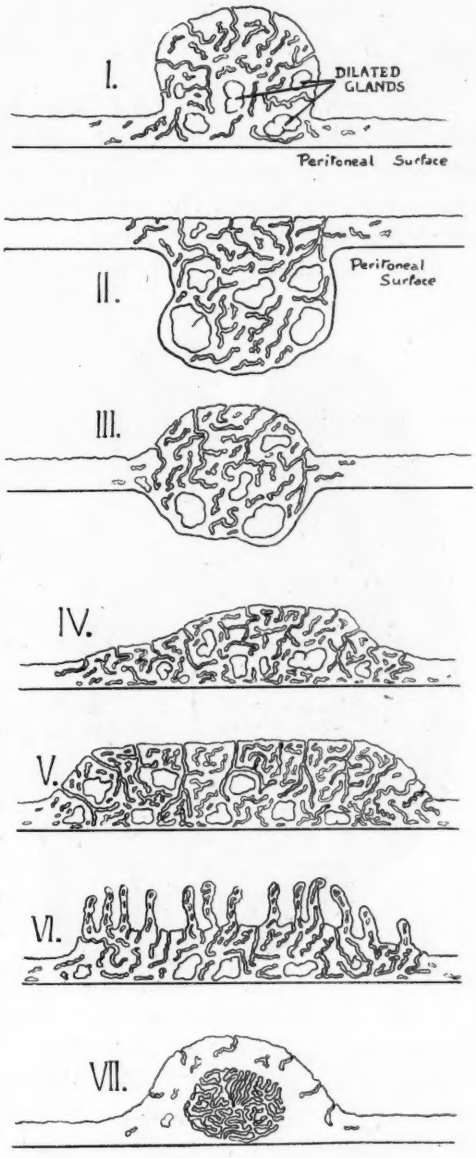

FIG. 235.—Diagram illustrating the various types of cholecystitis glandularis which have been encountered. I, Localized nodule projecting from the mucous surface; II, Localized nodule projecting from the peritoneal surface; III, Localized thickening of the wall causing a projection from both surfaces; IV, Intermediate form between the localized and diffuse types; V, Diffuse form; VI, Variety with papillary developments on the mucous surface; VII, Localized nodule in the wall, apparently unconnected with the surface (adenoma).

projection is usually sessile, but we have observed one example in which the base had a smaller diameter than the polyp, i.e., it was slightly pedunculated. The mass may become definitely pedunculated in a manner similar to the polypoid projections in the intestine. On gross section the tissue may be reddish, brown, greyish-white, or yellow in colour, and shows a number of open spaces.

The projection may take place into the peritoneal cavity (*Figs.* 234 II, 235 II). This is usually small and sessile. In one example the diameter of the base of attachment was equal to the diameter of the nodule. The peritoneum which covers the nodule is intact. The mucous membrane may be ulcerated, but is usually intact.

The thickening of the wall sometimes enlarges from the mucous as well as the peritoneal surface. This presents no special features, but combines those of the forms just described (*Figs.* 234 III, 235 III).

FIG. 236.—Specimen showing a localized area of cholecystitis glandularis at the fundus of the gall-blader.

These localized conditions merge into those in which a considerable portion of the wall is involved (*Fig.* 235 IV). Since the thickening is usually uniform, no projection is seen from the peritoneal surface, and the thickening appears to take place towards the lumen.

The generalized forms of cholecystitis cystica (*Figs.* 234, 235 V) may involve a considerable portion of the wall of the gall-bladder. We have observed, in one case, as much as three-quarters of the wall involved by this change. Rarely a papillary development into the cavity of the organ accompanies the changes in the wall, and may be recognized by a characteristic shaggy appearance when the projections are long, and a velvety form when they are short. This variety is the one which is most frequently regarded as carcinoma (*Fig.* 235 VI).

Occasionally a nodule of tissue is seen which does not possess an obvious connection with the lining epithelium (*Figs.* 234 VII, 235 VII, 236, 237). These cases, when not diagnosed as carcinoma, are referred to as adenoma. They are described as arising from 'aberrant gland tissue'. The undesirability and fallacy of such opinion will be discussed.

The cysts which occur in these tissues are usually small, though readily apparent, but sometimes they become large and constitute the major portion of the lesion. They contain fluid laden with cholesterol and, rarely, cholesterol concretions.[13, 24]

Microscopic Changes.—On microscopic examination a large number of closely intermingled changes are encountered. The most obvious is the

Epithelial Proliferation.—This activity of the epithelium is shown in two ways: (1) By downgrowth of the epithelium into the subjacent tissues; (2) By proliferation *in situ*, with multiplication of the layers of cells.

1. The downgrowth of the epithelium into the subjacent layers is the essential feature of the condition of cholecystitis glandularis. The glandular crypts retain the typical columnar epithelium with a definite basement membrane. There is no evidence of neoplasia; all suggestion of disordered growth and invasion with destruction of the surrounding tissue is absent.

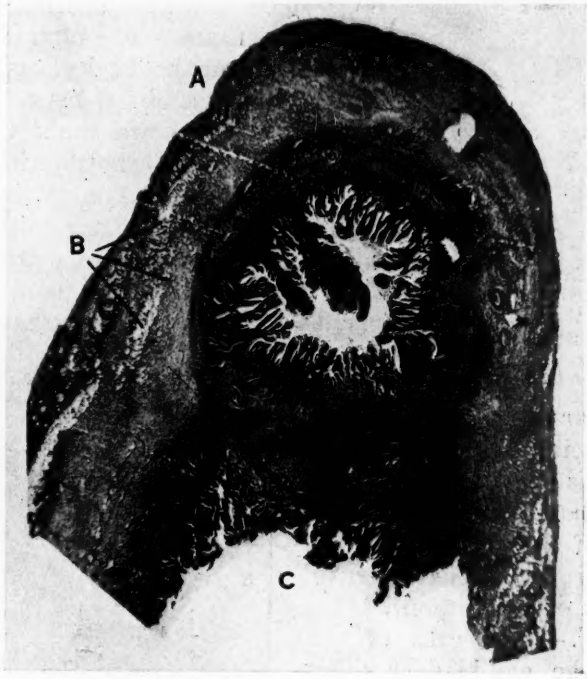

Fig. 237.—Section of the nodule in the fundus of the gall-bladder shown in *Fig.* 236. The connection of the epithelium of this nodule with that of the gall-bladder was shown by serial sections. A, Peritoneal surface; B, Fat; C, Cavity of gall-bladder. (× 3.)

The glandular crypts pass through the muscular coat and finally reach the subperitoneal layer. The course followed by these crypts is often very tortuous, and these tortuous portions cut in section give the appearance of numerous 'glands' (*Fig.* 244). The tortuosity of these crypts in the deeper layers is of paramount importance, since it may be assumed readily that there is no connection between the 'glands' observed in the deeper layers and the surface epithelium.

The cystic spaces, which are found particularly in the submucous and subperitoneal coats, are lined by a single layer of columnar cells, but in the larger cysts these become cuboidal or even flattened. Adjacent cysts may coalesce to form larger cysts (*Fig.* 238).

2. Local proliferation of the epithelium results in the formation of two or three layers. These are quite regular in their formation, however, both with regard to size, shape, and position, only a few mitotic figures being present and the basement membrane intact. Sometimes they approximate in appearance to squamous epithelium.[14]

FIG. 238.—Section of a localized nodule which projected from the peritoneal surface of the gall-bladder. A, Mucous membrane; B, Peritoneum. (× 6.)

These changes have been regarded as evidence of carcinomatous or, at least, precancerous development. There is, at present, no evidence for this assumption.

METAPLASIA.—The alterations of the epithelium from the typical gall-bladder type to varieties resembling cells typical of other portions of the bowel make the examination of the sections of cholecystitis glandularis a fascinating study. The types of epithelium found are: (1) Columnar epithelium with or without goblet cells—an epithelium of intestinal type; (2) Mucous glands; (3) 'Gastric' glands. These structures show the alteration of gall-bladder epithelium to various other forms of alimentary canal epithelium.

1. *Columnar Epithelium.*—In many of the epithelium-lined crypts the epithelium is of a tall columnar character, with basal nuclei (*Fig.* 241). The regularity of the size and position of these nuclei is a characteristic feature of many of the sections.

Goblet Cells.—The cells of the epithelium of the gall-bladder differ from those of the intestine in that all the cells produce mucin at the same time, but only in the form of small droplets. Thus in the normal gall-bladder goblet cells are infrequent. In the inflamed organ, however, goblet cells occur in a large proportion of cases.[14] These are to be found in most of the examples of cholecystitis glandularis.

2. *Mucous Glands* occur not uncommonly in chronic cholecystitis, having been found 185 times in 250 consecutive cases described by the writer elsewhere.[14] They occur in the

FIG. 239.—Portion of the thickened wall of a gall-bladder, showing the epithelium-lined crypts and the associated glands. (× 30.)

majority of the examples of cholecystitis glandularis, and were described in 1905 by Aschoff.[2]

They resemble mucous glands occurring elsewhere. The epithelial cells are arranged in small alveoli, the nuclei are round or oval and are situated in the middle of the cell, the position varying with the activity of the cells, and the protoplasm stains deeply with mucicarmine (*Figs.* 240, 243). There is no doubt that these glands arise from the surface epithelium either directly or from the crypts, since on section direct continuity of the epithelium can easily be traced.

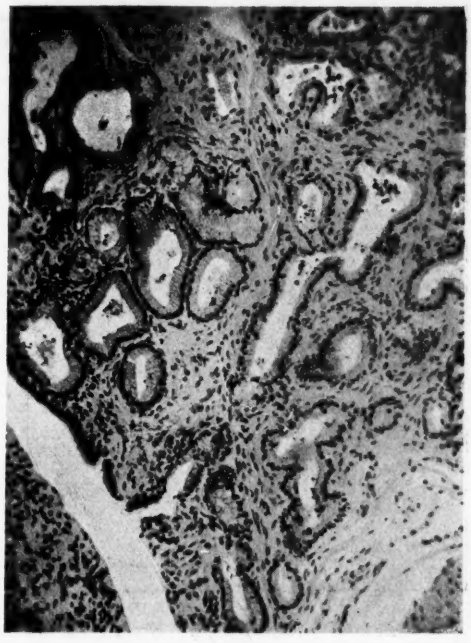

FIG. 240.—Higher-power view of the tissue shown in *Fig.* 239. (× 100.)

3. '*Gastric*' *Glands.*—In a number of cases of chronic cholecystitis in which mucous glands occur, other glands resembling the glands of the stomach and Brunner's glands of the duodenum are encountered. In structure they imitate mucous glands (*Figs.* 244, 249), but the alveoli contain clearer cells than those of the mucous glands, and the nuclei are crescentic in shape and situated in the basal portion of the cell. The protoplasm does not stain with mucicarmine. They are less common than the mucous glands, occurring in about 66 per cent of the cases in which these are found.[14, 19] They appear to arise usually by a modification of the mucous glands, but I have observed them in relationship with the gall-bladder epithelium without the intermediation of mucous glands.

FIG. 241.—Portion of an epithelium-lined down-growth showing the columnar cells resembling intestinal epithelium. The regularity of the size, shape, and position of the nuclei demonstrates the innocent nature of the epithelium. (× 810.)

RELATIONSHIP OF EPITHELIUM TO MUSCLE LAYER.—In order to reach the subperitoneal layer, the epithelial crypts penetrate the submucous and the muscular layers. The interruption of the muscular layer is a well-marked

FIG. 242.—Portion of tissue from an example of cholecystitis glandularis showing a 'lymphoid nodule'. (× 110.)

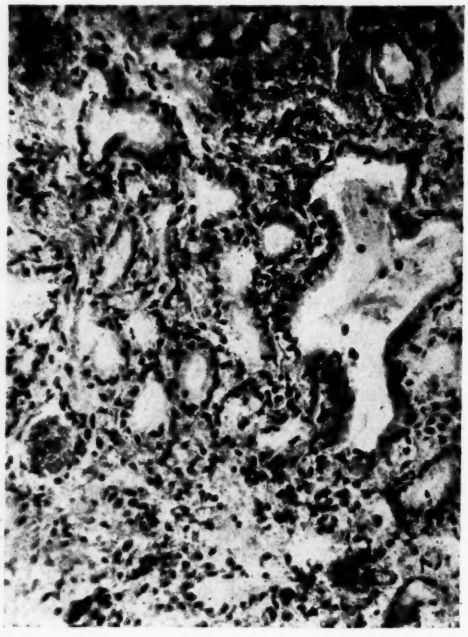

FIG. 243.—An area showing mucous glands. (× 160).

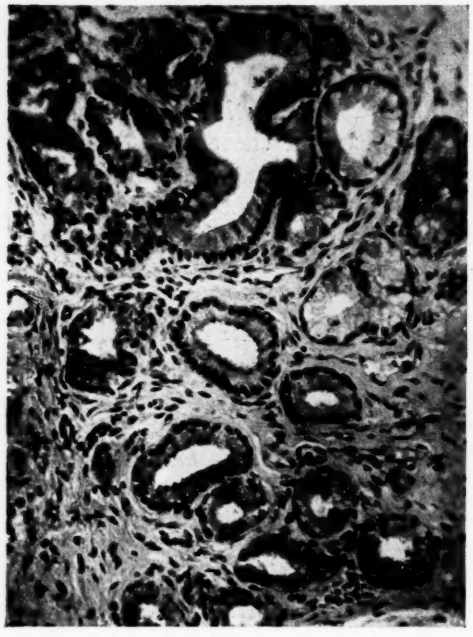

FIG. 244.—Section showing well-formed 'gastric' glands. (× 160.)

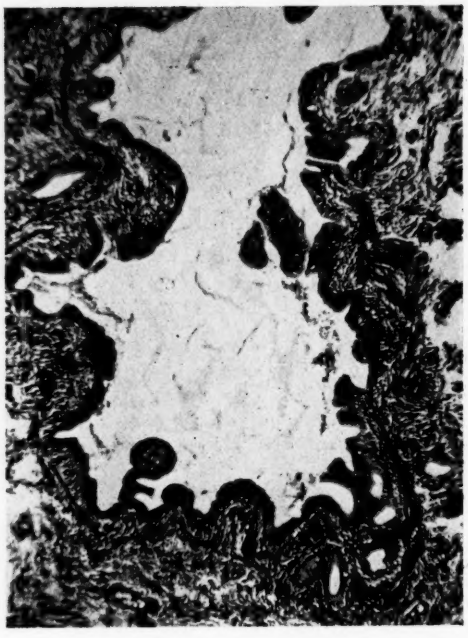

FIG. 245.—Epithelium-lined space in the wall of a gall-bladder showing the close association of the muscle tissue to the cavity. (× 40.)

feature of some sections (*see Fig.* 238). Frequently the muscle fibres are found to encircle, almost completely, groups of 'glands'.

There can be little doubt that in many of the examples of chronic inflammation of the gall-bladder there is proliferation of the smooth muscle. The amount of muscle in the wall of some of the thickened organs is much in excess of that found in the normal gall-bladder.

It is probable, therefore, that some of the muscle found around the epithelial groups is new formation; this opinion is expressed in the nomenclature used by some writers,[3, 20] 'adenomyoma', etc. It might be suggested that the arrangement of muscle around the glands is a response to function, i.e., new muscle is formed to give rise to a new small 'gall-bladder' in the wall of the organ (*Fig.* 245). On the other hand, the muscle lying around some of the larger groups probably arises from displacement of the existing muscle (*Fig.* 246).

FIG. 246.—Portion of the nodule shown in *Fig.* 236. There is some atypical proliferation of the epithelium, but the glands are well differentiated. The arrangement of these glands suggests that they are coiled tubes cut in many places. This is proved by serial sections. (× 85.)

In some examples the proliferation of the epithelium occurs for the most part on the mucous membrane aspect of the muscular layer, and in others it occurs largely on the peritoneal aspect. This relationship of the greater part of the proliferating epithelium to the muscular coat appears to be the circumstance deciding whether the nodule will project internally or outwards into the peritoneal cavity.

CONNECTIVE-TISSUE CHANGES.—The changes in the connective tissue (in chronic inflammation) may be considered in two groups: (1) Those apparently associated with the epithelial proliferation; (2) Independent changes.

1. Sometimes collections of round cells are found near the surface in association with epithelium which has become very similar to that of the bowel. These seem to correspond to the solitary nodules of the bowel (*Fig.* 242). This is, of course, hypothesis, but the association with the epithelium mentioned and the absence of other cells of chronic inflammation in the lymphoid collection are the reasons for the assumption.

Around the epithelial crypts the connective tissue may be of loose texture or definitely fibrous.

2. The proliferation of connective tissue cells observed in all chronic inflammatory conditions is found here, and may be extreme. On several occasions we have investigated gall-bladders, which we were convinced were

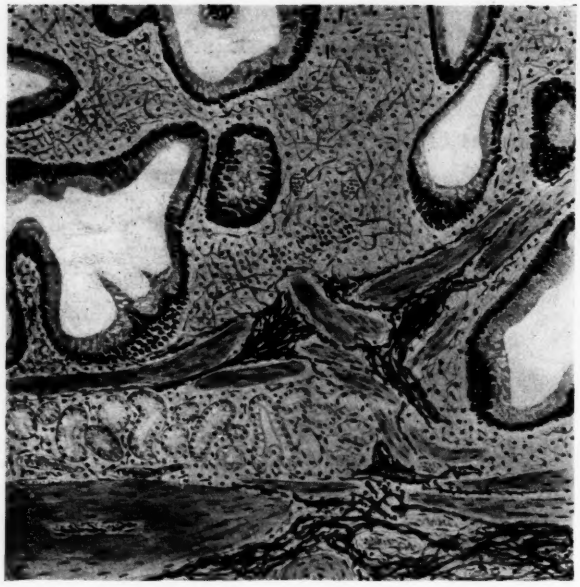

FIG. 247.—Portion of the wall similar to that shown in *Fig.* 246. Coiled tubules, cut in section, are present, principally of the mucous type, but also a few of the 'gastric' variety.

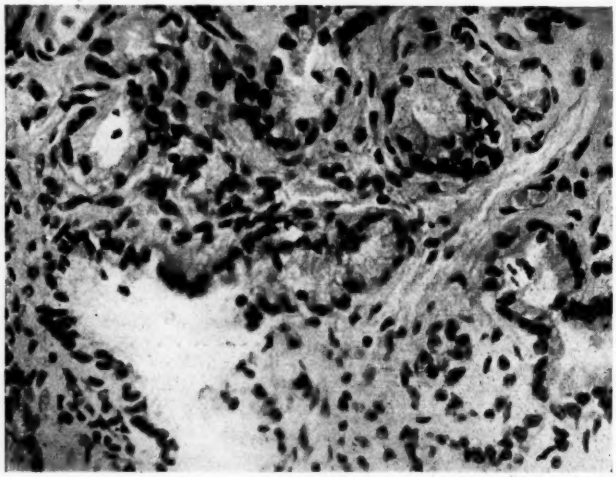

FIG. 248.—Photomicrograph showing the mode of formation of the glands as an outgrowth of a crypt. (× 200.)

of the cholecystitis glandularis type, but found only extreme fibrosis. Some of these, however, may be related, since in some cases evidence of the previous presence of glands is to be found in the occurrence of small spaces

sometimes still containing a few epithelial cells or of degenerating epithelial cells lying in the connective tissue.

The excess development of fat is striking in some organs, either as fat purely, or with a mixture of connective tissue. This tissue sometimes merges into lymphoid tissue, which, however, is distinct from the lymphoid nodules referred to above.

Any of these changes which occur in ordinary cases of chronic cholecystitis may be found in the condition described here.

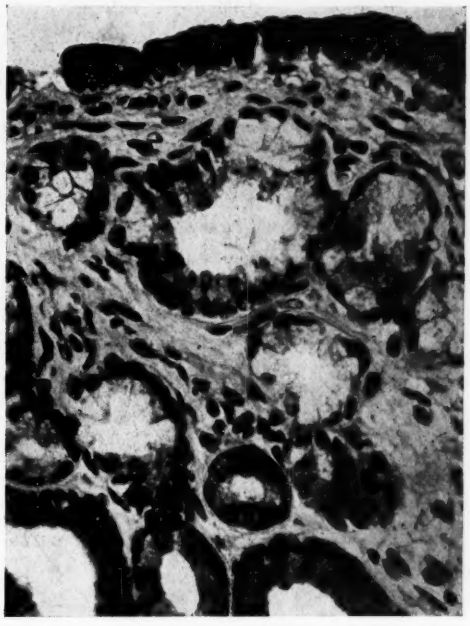

FIG. 249.—Higher-power view showing the structure of the 'gastric' glands. (× 360.)

Acute Inflammation.—When acute inflammation supervenes on chronic inflammation, the characteristic phenomena appear in the subepithelial tissues, and, depending on the degree of the stimulus and the time at which it was examined, hyperactivity and then destruction of the epithelium may be found.

The inflammation spreads down the crypts, and similar changes occur here. The destruction of the deeper epithelium may be an explanation of not finding this in cases where it was expected. In two cases of small abscesses in the wall of the gall-bladder, a few large epithelial cells were found, suggesting that the site of the abscess was originally an epithelium-lined space.

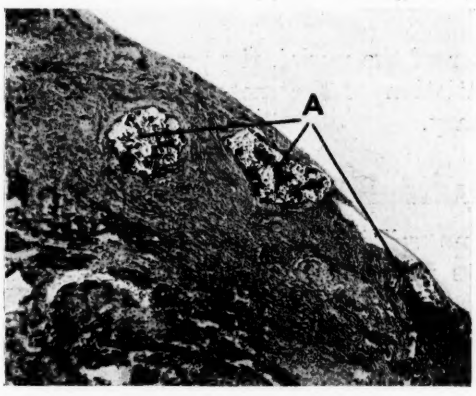

FIG. 250.—Small subperitoneal cysts containing cholesterol and bile pigment. (× 30.)

The relationship of the crypts to the peritoneum probably affords an explanation of the observation that some patients with acute cholecystitis have a peritonitis early, whereas others do not do so—excluding for the moment other factors, such as the virulence of the organism, etc.

Other Complications.—Obstruction of the cystic duct by a pedunculated 'adenoma' is described by the Mayos in Keen's *Surgery*. A calculus in a cyst in the wall of the gall-bladder may be mistaken for a calculus in the cavity of the gall-bladder.

Relationship to Malignancy.—This problem, as in all parts of the body, is extremely difficult, and apparently convincing arguments may be offered for diametrically opposed opinions.

It seems to us reasonable and probable that neoplastic development could arise in the epithelium of cholecystitis glandularis. On the other hand, we have not observed, in the few examples that have come to our notice, any instance of changes which would withstand critical examination by the usual criteria for malignancy. The regular arrangement of the cells, the

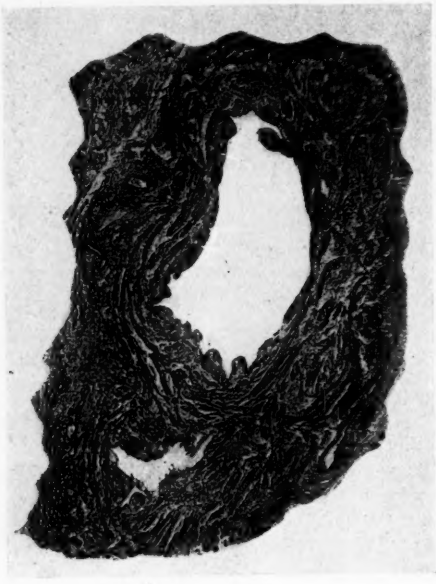

FIG. 251.—Portion of a wall of a gall-bladder showing cystic spaces which are not lined by epithelium. The organ had been the site of both chronic and acute inflammation, and the cysts were probably lined previously by epithelium which had been destroyed. (*See Fig.* 252.) (× 11.)

FIG. 252.—Higher-power view showing the nature of the lining of the cysts seen in *Fig.* 251. The greater part of the cavity of the gall-bladder had a similar lining. (× 75.)

normal polarity and the regular character of the nuclei, the presence of basement membrane, the degree of differentiation of the metaplastic glands all militate against a diagnosis of malignancy.

CLINICAL CHARACTERISTICS.

Cholecystitis glandularis presents no special clinical features. It has been observed, in this series, in patients whose ages ranged from 38 to 72. All the patients were females.

In every case the gall-bladder was removed on account of signs and symptoms of chronic cholecystitis; in 9 of them acute inflammation had supervened.

Gall-stones were present in 21 out of the 25 cases. In the 4 other cases, record of the presence or otherwise of stones was absent.

Its greatest importance rests in its possible confusion with malignant disease. A thickening of the wall, particularly when considerable fibrosis rendered this very hard, and nodular projection several times simulated and

led, at operation, to the provisional diagnosis of malignancy. Even microscopically two cases were returned as carcinoma. The subsequent history shows that the patients have had no ill effects after a period of seven years, even though in one case the thickening in the wall, examined microscopically, extended for 2 in. along that aspect of the wall which was in contact with the liver.

As stated, the condition was found in 9·5 per cent of 400 gall-bladders examined, but this result cannot be accepted as an indication of the frequency of occurrence, since the cases were, unintentionally, picked. For example, in addition to material derived from hospital and our own practice, a number of the specimens were sent to the writers by colleagues (to whom they would express their grateful appreciation) who knew of the interest evinced by us in the subject, and other 'less interesting' material was not examined.

In comparison with this, there are the figures of 'innocent tumours' observed by other writers :—

Mayo - -	107	examples of papilloma in	2538	gall-bladders	(4·21	per cent)
Irwin and McCarty[11]	85	,, ,, ,,	2168	,,	(3·92	,,)
Abell[1] - -	8	,, ,, tumours in	288	,,	(2·78	,,)

The difference between these and the figures of this paper is due in part to the 'picking' of cases described here, and also to the inclusion of examples showing a degree of development insufficient to give rise to a diagnosis of neoplasm.

DISCUSSION.

The importance of grouping the various forms of this condition together is shown by the many opinions—as expressed by the terminology—promulgated regarding its nature. The hypotheses put forward are that it is : (1) Heterotopic tissue displaced in fœtal life, i.e., a cell rest. (2) Neoplastic development—(*a*) malignant, (*b*) innocent. (3) A precancerous change.

1. **Heterotopic Tissue Displaced in Fœtal Life.**—The brilliant hypothesis of Cohnheim that masses of aberrant tissue resulted from the segregation of cells during fœtal life and that tumours could arise from these has gained a firm hold on pathological opinion. However, careful examination of structures apparently conforming with this suggestion demonstrates that all gradations may be found from the normal through minor alterations up to the fully developed lesion. This is shown particularly well in the epithelial proliferations in the wall of the gall-bladder.[14, 19] In all cases multiple or serial sections show that the deeper 'glands' are continuous with the surface epithelium and apparently develop from it.

2. **Neoplastic Change.**—

a. The absence of the criteria of malignancy has been considered.

b. Innocent growth (adenoma) may be excluded by the observations : (i) A definite etiological factor—the chronic inflammation—is to be observed in the surrounding connective tissue. (ii) There is no real encapsulation of the epithelial glands ; they definitely grow into the wall of the organ, though without destruction of tissue. (iii) The amount and degree of differentiation of the heterotopic tissue present does not occur usually in growths.

3. **Precancerous Changes.**—It cannot be denied that the epithelial proliferation may, in late stages, give rise to malignant development. There seems no reason to suppose, however, that this would occur more readily or more frequently in cholecystitis glandularis than in ordinary cholecystitis. There has been no suggestion of malignancy in any of the cases which we have observed.

The exclusion of these various hypotheses necessitates their replacement by an alternative. The theory of metaplasia (heteromorphosis) is now on a well-established basis. Tissue of one type often changes to another related form, probably by de-differentiation of the cells at first, followed by re-differentiation. Any related form of tissue may arise. The epithelium of the gall-bladder arises from that of the primitive alimentary canal, and may, given the suitable stimulus, return to a primitive form. When this differentiates once more, it may form, not typical gall-bladder epithelium, but, depending on the stimulus, epithelium resembling the cells and structures resembling those of the stomach, duodenum, or intestine.

Proliferation of connective tissue as the result of chronic irritation is a well-recognized phenomenon, but epithelial proliferation in similar circumstances, though sometimes more important, is often not appreciated.

In several parts of the body, but particularly in the stomach, this epithelial proliferation associated with chronic inflammation has been interpreted as carcinoma or as precancerous, so that very high proportions of gastric ulcers were thought to be malignant. Critical examination has shown this view to be inexact.

The proliferative epithelial changes in the gall-bladder should be regarded as the reaction of the epithelial cells to the chemical stimuli occurring in an inflamed gall-bladder.

SUMMARY.

1. A number of examples of diffuse or localized thickening of the wall of the gall-bladder which are honeycombed by epithelium-lined crypts and glands are described.

2. Some of these cases conform with the condition described by Bodnár as 'cholecystitis cystica', but since others present the characteristic involvement of the wall without cyst formation, the term 'cholecystitis glandularis proliferans' is applied.

3. Several types, which depend on the site of the epithelial development, are described.

4. They develop as a result of epithelial proliferation with metaplastic change into various types of alimentary canal glands.

5. It is not malignant, and the diagnosis from malignancy is important, but easy when the nature and characteristics of the condition are understood.

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VISITS TO SURGICAL CLINICS AT HOME AND ABROAD.

DR. MURK JANSEN AND HIS CLINIC AT LEIDEN.

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Dr. Murk Jansen, the leading orthopædic surgeon of Holland, is well known amongst British surgeons as a researcher, philosopher, and practical surgeon (*Fig.* 253). He had the advantage (as every specialist should) of a very thorough grounding in general principles; after over four years' post-graduate work as prosector of anatomy, and as an assistant in internal medicine and general surgery, he studied in Vienna and in Würzburg, and practised internal medicine and orthopædics for some years in order to obtain a sound insight into the fundamental principles of pathology and diagnosis. The special study of orthopædics attracted him, as he realized the scope that this specialty offered for original investigation; and, as opportunity offered, he devoted himself entirely to orthopædic work. About this time he was invited to become Lecturer in Orthopædics at the ancient university of Leiden; he took up his abode in that city, and has remained there ever since. He has a few beds in the University Hospital, which is a large state-run institution to which all persons have the right of admission; and he has over sixty private beds in the Anna Kliniek voor Orthopaedie (*Fig.* 254), which is a private hospital for the treatment of paying patients.

This beautiful little hospital, which will form a model, it is hoped, for all others in Holland, was opened on Nov. 11, 1929. It stands upon the outskirts of the city, in its own grounds, surrounded by an orchard and a garden, and is as perfect as a combination of surgical and architectural skill could make it. Apart from a few patients transferred from the University Hospital, who pay for extras only, all patients pay; they are divided into five classes, paying from 2.50 to 10.50 guilders per day (12 g. = £1), and are housed in private rooms and small wards of two, three, or four beds. A very large, light operating-theatre (*Fig.* 255) and a plaster-room (*Fig.* 256) are provided, and the hospital has its own instrument-shop, which employs thirteen men, and produces all the splints and instruments needed by the patients. The nurses are state-registered, and receive a three-years' training.

Dr. Jansen has a very large hospital and private practice, patients coming to him, not only from all parts of Holland and Belgium, but also from more distant countries. Dr. Fransen, his partner, assists him in all his work, public and private, and sees all out-patients at the University Clinic; he also

performs a number of operations. Dr. Jansen sees private patients daily at his house from 1 to 3 p.m., and his organization for dealing with a large number of patients is very interesting; the histories are prepared by his assistants, the patients are made ready for him to examine in a number of rooms and cubicles, a card-record of each case is placed in readiness on the door, and X-ray and other investigations are made on the spot as required.

Numerous operations are performed; at the Anna Kliniek alone, 1057 operations have been carried out in the main operating-theatre during the past year and a half. The technique and instruments used are practically

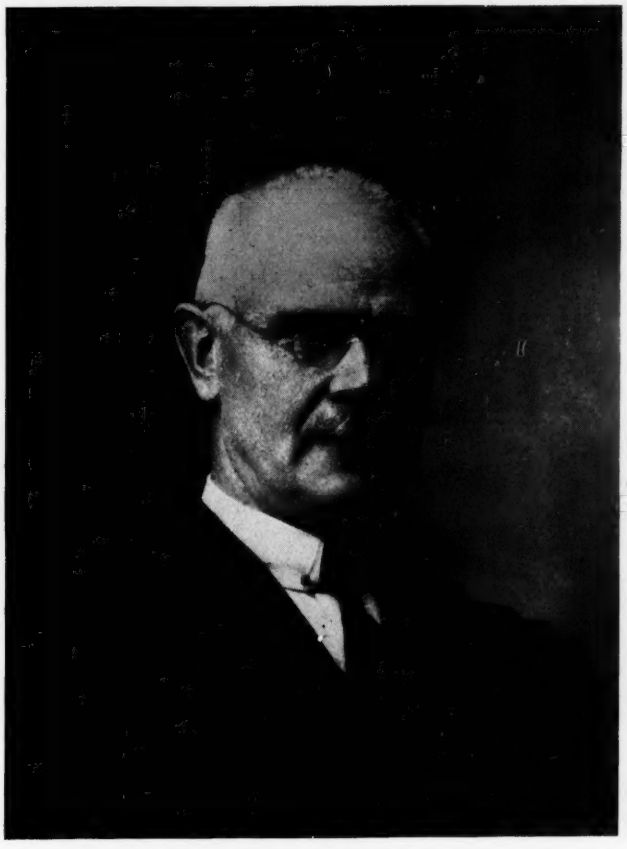

FIG. 253.—Dr. Murk Jansen.

identical with those employed in this country. The rubber gloves are dry-sterilized by the vapour of paraform tablets, the various sizes of gloves being stored on metal trays in a cabinet somewhat resembling a microscope-slide cabinet; the tablets are changed every three or four months, and I was told that there has never been the slightest anxiety about the sterility of the gloves prepared in this way. Forty-eight hours' exposure is allowed for the sterilization to take place. Alcohol is largely used for the sterilization of apparatus, and of the operator's skin; and Kirschner's method, with a 7·5 per cent solution of tannic acid in alcohol, is exclusively used for the final cleansing

of the patient's skin, following the usual treatment with soap, spirit, and ether; the tannic acid method is stated to be superior to all others in its efficiency and freedom from production of dermatitis.

Three operations were seen :—

Operation 1.—Man, age 67. Bucket-handle tear of semilunar fibrocartilage; no tourniquet used in this particular case because of cardiovascular degeneration. Rather long curvilinear horizontal incision; gauze skin-guards; dry gauze swabs; fibrocartilage excised with a long, narrow, sharp-pointed Adams' knife; catgut ligatures and capsule-suture; linen-thread in skin; wire cradle back-splint for ten days, then active exercises.

Dr. Jansen is a vigorous opponent of the indiscriminate use of massage, considering that far better results are attained at far less cost by the energetic exercising of the patient's muscles by active voluntary exertion. He

FIG. 254.—Anna Kliniek voor Orthopaedie, Leiden.

holds that massage and electrical treatment are often exploited unnecessarily, and are foisted somewhat unscrupulously on a gullible public; he uses massage and electricity, of course, where they are definitely indicated, but he lays it down as a general principle that no method of treatment should ever be employed without a clear understanding of its mode of action and of its purpose, and without a clear indication for its use. He believes and teaches that failure to observe this principle is largely responsible for the absence of any striking recent advance in therapeutics.

Operation 2.—Woman, age 51. Re-operation for hallux valgus, after unsuccessful operation elsewhere. Infiltration analgesia with about 25 c.c. of 0·5 per cent novocain solution. Base of proximal phalanx removed with very sharp and powerful bone-cutting shears. Triangular flap of capsule, V-shaped, pointing proximally, sutured well back on inner side of toe, to

maintain adduction afterwards; abductor hallucis tendon then sutured to this, after transplantation, to overcome the rotation of the toe which is found always to occur in these cases.

Dr. Jansen said that he found the removal of a good-sized piece of the base of the proximal phalanx (the operation introduced into England by Davies-Colley, and known by his name) was in every way a most satisfactory proceeding.

Operation 3.—Woman, age 27. Progressive muscular dystrophy. A standard Naughton Dunn stabilization, combined with a posterior bone-block, after the style of Willis Campbell, was performed. The special feature of this case was the method of dressing immediately after the operation; gauze, about ½ in. of absorbent white cotton-wool, and an ordinary open-wove

Fig. 255.—The operating-theatre in Dr. Jansen's clinic.

bandage, were applied; then a further layer, at least 1¼ in. thick, of very good non-absorbent wool, and finally a bandage of tubular stockinette applied exceedingly tightly; the tourniquet was then removed. It was stated that this method entirely prevented hæmatoma and post-operative pain, the foot being almost as firm as if it were encased forthwith in plaster-of-Paris. The foot was then placed in an ordinary wire cradle-splint, and plaster would be applied after the skin sutures had been removed in about a fortnight's time; this plaster would be taken off after six weeks, and the patient would then be allowed to walk on a second and final plaster, kept on for two months.

After the operating session, photographs and radiograms of a case of congenital absence of the sacrum ('asacria') were shown. This rare developmental

abnormality has been observed and described once before by Dr. Jansen. The buttocks are notably small, the anus deep, and the child, if male, sits on the scrotum. The radiogram shows complete absence of the sacrum, and the presence of lumbar spina bifida; the father also has spina bifida. The condition is attributed to smallness of the amniotic sac at an early stage, before the period of infolding.

In the wards were shown a number of interesting orthopædic cases. Amongst these was one of claw-hand, the result of progressive muscular dystrophy, in which arthrodesis of the proximal interphalangeal joint of the fourth finger had been performed in order to restore grip. For claw-toes it is Dr. Jansen's practice, in suitable cases, to arthrodese the proximal

FIG. 256.—The plaster room at Dr. Jansen's Clinic.

interphalangeal joint in order to allow the long flexors to flex the metatarsophalangeal joint; without arthrodesis, the lumbricals and interossei hyperextend the toes at the basal joints in claw-foot.

Dr. Jansen has wholly abandoned the use of remedial exercises in the treatment of scoliosis and kypho-lordosis, and has substituted for it the wearing of a simple appliance which may be called his 'mental educator'. (The strict translation of its Dutch name is 'straight reminder', the instrument being intended to remind the patient to stand straight.) It consists of a light pelvis-band, to which is riveted an upright metal bar, exerting slight pressure by means of a pad upon the maximum convexity, and having a narrow leather strap around the neck. The patient is thus constantly reminded to make a corrective muscular effort, so as to avoid the pressure of the pad upon the convexity. It is found that after the educator has been

worn for a year or more, marked improvement occurs, and by this means the treatment of scoliosis and kypho-lordosis is enormously simplified and cheapened, especially in the case of patients living at a considerable distance from the clinic. Apart from a plaster-bed for lateral recumbency employed by night for scoliosis, no corset or appliance of any kind is used other than the educator. Dr. Jansen teaches that anything that even marks the skin of the thorax or of the abdomen is bad. He considers that the improvement in posture and in the tone of the abdominal muscles produces a negative pressure in the upper part of the abdomen; and this negative pressure (whose existence has been demonstrated by manometric readings taken with a colonic tube) causes engorgement of the liver and other vital organs with healthy blood. This accounts for the marked improvement in general health that is invariably observed as posture improves.

Another interesting out-patient case was that of a girl aged 10 years, having weak muscles, slight knock-knee, and genu recurvatum, who complained of a sensation as of something becoming caught between her femur and her patella. No foreign body or loose body was present, but a lateral radiogram showed flattening of the femoral condyle, and a sloping of the upper surface of the tibia backward and downward. The epiphysial ends both of the femur and of the tibia appeared to have swung backward, the former upward and the latter downward, so that the joint-space had become narrowed in front. Dr. Jansen explained that this led to the patella becoming unduly high, the fat-pads becoming prominent in front and liable to be nipped; this explained the patient's symptom. He has described this condition as 'patella alta spuria', in contradistinction to 'patella alta vera', in which the patellar ligament is abnormally long.[1]

A number of other interesting cases were seen, some of which gave Dr. Jansen an opportunity of expounding, very lucidly and convincingly, his well-known theory of the causation of a number of obscure developmental abnormalities, such as achondroplasia, osteogenesis imperfecta, etc.[2, 3]

On Thursday, May 21, 1931, an interesting little ceremony was performed at the Anna Kliniek voor Orthopaedie. Dr. Jansen unveiled a bronze plaque of Sir Robert Jones which has been erected on the main staircase of the hospital, and delivered a short address, in which he described the great part played by Sir Robert Jones in the development of the science of orthopædic surgery. Sir Robert Jones, who was supported by several other British orthopædic surgeons, made a suitable reply.

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SHORT NOTES OF RARE OR OBSCURE CASES

AN EXAMPLE OF BENIGN OSTEOGENIC SARCOMA.

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The advantages accruing from reporting cases of rare conditions such as bone sarcoma are demonstrated by the conclusions which have been drawn from the specimens in the American Registry. Any example of malignant tumour of bone is worthy of record, and particularly one which illustrates some special feature. For this reason the following case is described :—

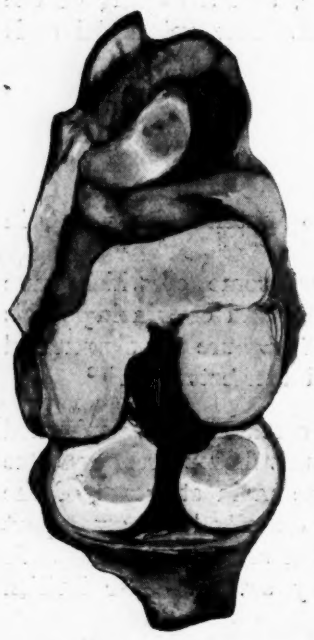

Fig. 257.—Drawing showing the knee open at operation. The small tumour is presenting between the condyles of the femur, arising from the outer condyle.

M. D., male, age 19, reported for examination on account of a generalized swelling of his left knee of about twelve months' duration. During the four or five months prior to examination the knee had become puffy, and although there had been but little pain, the leg was unable to support the weight of the body. There had been some pain on movement.

On Examination.—The left knee was swollen and puffy, with no obvious fluid. The lower end of the femur was slightly tender over the outer condyle, but with little tenderness over the joint. There was no crepitus, and marked limitation of movement, accompanied by pain. All the other joints of the body were normal. The lungs were normal, both on clinical examination and by X-ray. The X-ray of the knee-joint showed erosion of the inner aspect of the outer condyle of the femur. The pre-operative diagnosis was tuberculosis of the joint.

Operation.—A distal horseshoe incision was made, and the flap of skin and subcutaneous tissue turned upwards. The patellar tendon was incised with the expansion of the vasti, and the patella was turned upwards. A small growth, bluish in colour, was present situated in the intercondylar space. It was springing mainly from the outer condyle. The outer condyle together with the tumour and portion of the inner condyle (by means of a step-cut) were removed (*Fig.* 257). The upper surface of the tibia was also removed.

FIG. 258.—Cellular area of the tumour with osteoid tissue. The sarcoma cells are curiously uniform in size and shape and the nuclei less vesicular in appearance than is usual. Three foreign-body giant cells are present. (× 80.)

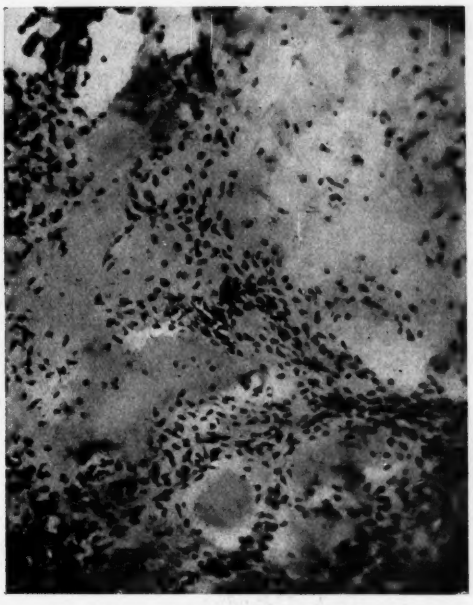

FIG. 259.—Photomicrograph of another area of the growth similar to that shown in *Fig.* 258, but with a greater proportion of osteoid tissue. (× 80.)

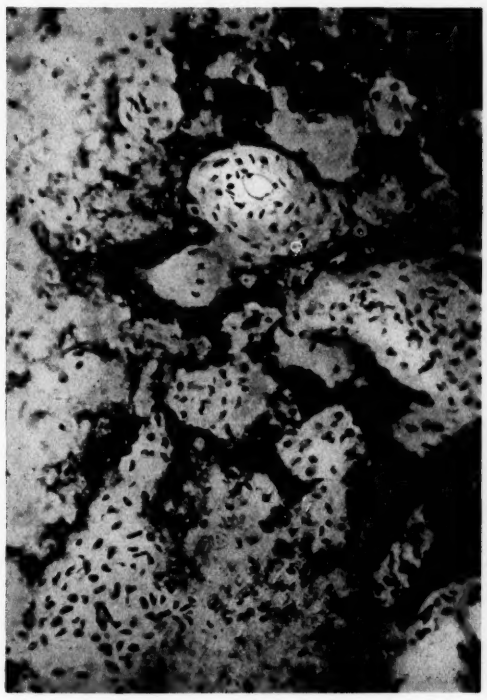

FIG. 260.—Calcification in osteoid tissue with a certain amount of bone formation. A few osteoblasts may be seen. (× 80.)

FIG. 261.—Photomicrograph of another portion showing cellular tissue, osteoid tissue, and bone. (× 80.)

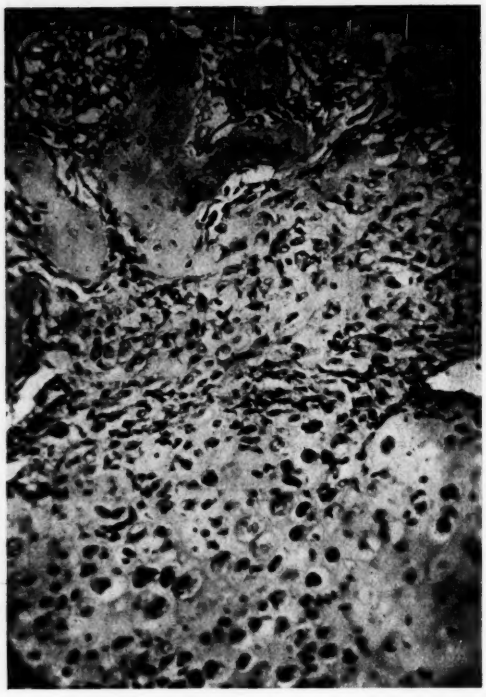

FIG. 262.—Osteoid tissue, cellular tissue, and cartilage. The cells in this part are more 'active'. (× 80.)

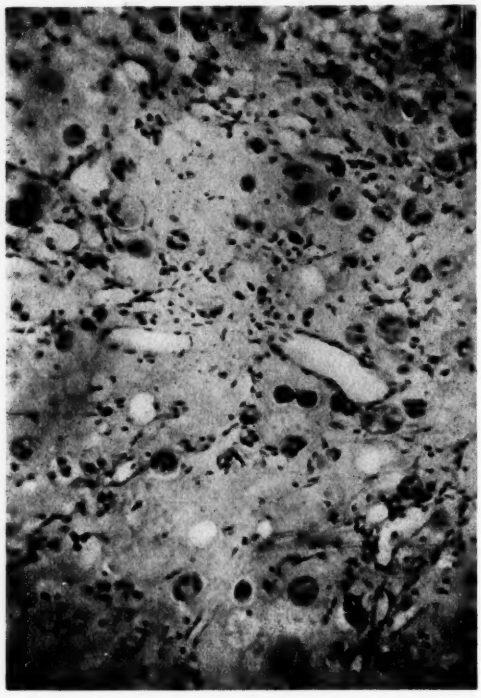

FIG. 263.—Another portion showing actively growing cartilage. (× 80.)

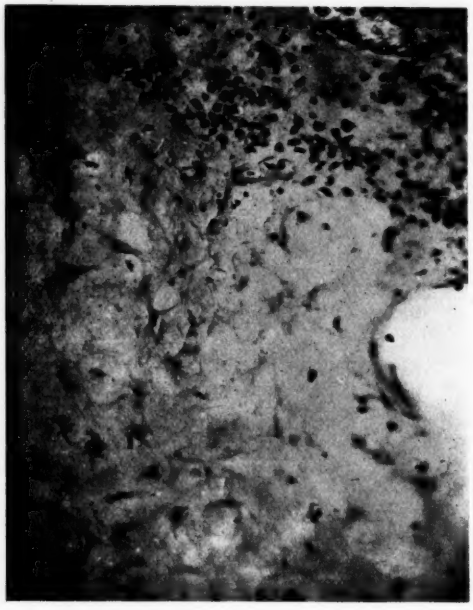

FIG. 264.—Photomicrograph of a section showing cellular tissue merging into mucoid connective tissue. (× 80.)

PATHOLOGICAL EXAMINATION.—

Macroscopic Appearance.—The specimen consisted of the outer condyle of the femur and portion of the inner condyle, together with the tumour which was growing from the medial aspect of the outer condyle. The growth measured 1½ in. in diameter and about one-third of its mass projected from the surface of the bone. It was much softer than ordinary bone, small areas of mucoid change being present, and spicules of bone and calcified material were present throughout the growth.

Microscopic Examination.—The growth showed all the characters of an osteogenic sarcoma: (1) Areas of cellular activity, the cells being for the most part of the spindle variety (*Fig.* 258). (2) Formation of osteoid tissue occurred in many areas (*Fig.* 259). (3) Calcification both of the osteoid tissue and of the ordinary tissue occurred (*Fig.* 260). (4) Ossification was present in some areas (*Fig.* 261). (5) Cartilage was present in some portions (*Figs.* 262, 263). (6) The spindle-cell tissue merged into typical mucoid tissue (*Fig.* 264). (7) In some areas many giant-cells were found. (8) In some areas the tissue was more vascular and many cells indistinguishable from cells of the bone-marrow (including myelocytes) were present.

SUBSEQUENT HISTORY.—The patient recovered rapidly from the operation, and bone union had occurred at the end of two months. Nine years later the patient is perfectly well—the local condition of the knee region is satisfactory, without sign of recurrence, and the lungs are clear.

COMMENT.

Though the great majority of primary tumours of bone are malignant, some intensely so, a few examples of benign growths have been recorded.

The case described is of interest since no recurrence followed on even very local removal. The microscopic picture showed that the tumour was a typical example of an osteogenic sarcoma. Such a benign course suggests that the tumour might possibly show some distinct morphological differences from other osteogenic sarcomata. Careful examination of the sections showed that the cells were curiously uniform in size and shape and that giant cells present were of the foreign-body type.

Even had this been noted nine years ago it is doubtful whether the bad prognosis then given would have been modified. It suggests, however, that such benign cases should be carefully examined for some such morphological peculiarity. Information is difficult to obtain concerning these tumours owing to their rarity, and only the careful examination of those which do arise will advance our knowledge.

From the point of view of treatment, the question has often arisen: Is it not desirable to treat most sarcomata conservatively by, at least, amputation close to the lesion? Extensive operations occasionally are followed by a cure—but do not these tumours belong to the variety described here? We know that extensive operations in malignant cases will not cure the condition owing to the presence of metastases in the lungs. On the other hand, the less radical methods of treatment will save unnecessary mutilation in the comparatively benign cases.

EXCISION OF SUBCLAVIAN ANEURYSM ASSOCIATED WITH CERVICAL RIB.

By WILLIAM BILLINGTON,
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DEFINITE aneurysm of the third stage of the subclavian artery associated with cervical rib is a very rare condition, and excision of such an aneurysm with relief of symptoms must be almost unique.

HISTORY.—The patient was a single woman, 42 years of age, who had enjoyed good health until the onset of her present symptoms. For several years she had complained of pains in the back and under the left shoulder, for which no clear explanation was found. In May, 1930, her doctor discovered a definite pulsating lump above the left clavicle, and she then complained of pain in her left arm, and it was noticed that there was a difference in the timing of the radial pulses. A month later the radial pulse on the left side had disappeared, the arm felt cold, and the pain in it had become severe.

FIG. 265.—Fully developed right cervical rib; left cervical rib (indicated by arrow) incomplete.

ON ADMISSION.—In November, 1930, the patient was admitted into my wards at the Queen's Hospital. She was a poorly-nourished woman, but was organically sound. She stated that in May, 1930, her left arm started to ache and the pain had gradually become worse. It had also extended to the shoulder and the left side of the neck. The pain increased when she was at work and especially so when she lifted heavy weights, such as a pail of water. She had no pain at night, or when the arm was at rest. The fingers of the left hand felt cold and numb, and sometimes they went quite white.

ON EXAMINATION.—A swelling could be felt above the left clavicle. It was elongated, about 2½ in. in length, and at its centre about the size of a walnut. No pulsation could be felt in it. The swelling could be moved up and down, but only slightly from side to side. When the shoulder was raised the swelling slipped under the clavicle, and part of it could be felt beneath the pectoralis major and internal to the coracoid process. There was no

evidence of median or ulnar paralysis. The radial pulse could not be felt, and the tips of the fingers were cold. No weakness of the arm existed. A Wassermann test was negative.

X-ray Report.—Dr. J. Brailsford took an X-ray photograph and reported upon it as follows: "The radiograph shows a fully developed right cervical rib. The left cervical rib is incomplete; its anterior extremity has formed a symphysis with the first rib on a plane with the clavicle, indicated by an arrow (*Fig.* 265). The swelling in the soft tissues is in this area".

Operation.—A curved incision about 4 in. long was made parallel with and a little above the clavicle in its outer part, and extending vertically upwards at its inner end over the posterior margin of the sternomastoid muscle. The lump was readily exposed and found to be an aneurysm of the subclavian artery. It commenced at the outer edge of the scalenus anticus, where the artery was at a much higher level than is normal, making the long axis of the aneurysm almost vertical. There was no pulsation in the sac. The lowest trunk of the brachial plexus was adherent to the outside of the sac, and moved with it. The vessel at either end of the aneurysm was tied with a double catgut ligature, and the aneurysm was excised. As the cervical rib did not appear to be interfering with the nerves of the brachial plexus, it was not disturbed.

Fig. 266.—The aneurysm.

Report on the Aneurysm (Dr. Neale, Pathologist to the Queen's Hospital).—"The portion of the artery removed is approximately $2\frac{1}{2}$ in. in length and shows a fusiform dilatation reaching a maximum diameter of $\frac{3}{4}$ in. At the place of maximum dilatation the external surface of the artery feels thin, and foci of hæmorrhage are seen in the adventitial tissue. The lumen is largely occupied by a laminated thrombus formation through which, however, a minute channel is detectable. (*Fig.* 266.)

"Microscopically, the muscular coat shows a slight degree of fibrotic change without evidence of inflammation. The internal elastic lamina at one place is duplicated and fragmented, and at this site thrombosis has occurred, showing as a laminated deposition of fibrin—the deeper layers of which show fairly advanced organization and canalization. There is no primary disease in the intimal layer of the artery. The findings are consistent with traumatic injury to the artery."

Subsequent Progress.—The patient made an uneventful recovery, and all pain in the shoulder and arm disappeared. The pain was apparently caused by pressure upon the lowest trunk of the brachial plexus by the sac of the aneurysm, especially when the latter was pulled upon by lowering of the shoulder.

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A CASE OF SUPPURATIVE PYLEPHLEBITIS SECONDARY TO CARCINOMA AT THE DUODENAL BILIARY PAPILLA.

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AND T. B. DAVIE,

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THE condition of suppurative pylephlebitis with generalized abscess formation throughout the liver, resulting from the obstruction to the opening of the ampulla of Vater by a carcinoma at this orifice, is of sufficient rarity in our opinion to warrant the publication of the following case :—

HISTORY.—The patient, a male of 51 years, had been investigated in hospital for two transient attacks of jaundice, each lasting a week, with a six-month period of freedom from symptoms between attacks. During the attacks there was slight aching pain in the right upper quadrant of the abdomen, and investigation showed enlargement of the liver, the anterior edge reaching down nearly to the umbilicus. The liver was smooth, rather soft, and not tender. Examination by Graham's method showed failure of the gall-bladder to fill with dye, and van den Bergh's test was strongly suggestive of obstructive jaundice. However, the relative absence of pain and the success of medical methods in clearing up the jaundice led to the diagnosis of catarrhal jaundice, and he was discharged from hospital. One month later he was re-admitted suffering from severe colicky pain of sudden onset in the upper abdomen, intense jaundice, fever, and with a history of a rigor on the day previous to admission.

ON ADMISSION.—Intense jaundice, temperature 102·6°, pulse 100 ; liver enlarged to below the umbilicus, slightly tender—more so over gall-bladder area—smooth, and somewhat soft. Gall-bladder not palpable. Epigastric and right hypochrondriac tenderness and rigidity. Blood : white-cell count 22,000 per c.mm., mostly polymorphonuclears. Another rigor occurred shortly after admission to hospital. A diagnosis of suppurative cholangitis was made, obstruction to the common bile-duct by calculus being considered probable, and drainage of the gall-bladder was decided upon.

OPERATION.—Through a right-sided paramedian incision, centring at the umbilicus, the gall-bladder was exposed. This viscus was found to be markedly distended and thin-walled, and concealed to palpation by the enlargement of the liver. The liver was smooth and intensely and evenly jaundiced, and no abscesses were visible. No calculus was palpable in the gall-bladder, nor in the cystic and common bile-ducts. The pancreas felt firm but not malignant. Continuous with the head of the pancreas was felt a rounded firm mass apparently indenting the second part of the duodenum or protruding into its lumen. Investigations were hurried because of the precarious state of the patient under the anæsthetic. After packing off the peritoneal cavity, a large tube was inserted into the gall-bladder and much foul-smelling pus mixed with 'white bile' was evacuated. The abdomen was

closed, leaving a drainage tube in the right kidney pouch in addition to the cholecystostomy tube.

Post-operative History.—Bile commenced to flow from the cholecystostomy tube a few hours after the operation, and continued to do so up to the time of his death five days later. Although the patient felt relieved and his jaundice was considerably diminished, his general condition became steadily worse. Auricular fibrillation supervened two days later and was only with difficulty controlled by digitalis. Uræmia-like symptoms followed, his blood N.P.N. being 120 mgrm. per cent; and death occurred five days after the operation, being preceded by muscular twitchings, anuria, and coma.

Autopsy.—At the post-mortem examination the enlarged, intensely jaundiced liver was found to weigh 71 oz. Scattered over the surface were numerous small whitish areas, especially noticeable along the anterior edge. These resembled multiple malignant metastases, but proved to be the larger of very numerous abscesses present within the organ, as well as on its surface. Microscopically the abscess formation was associated with the portal tract. In this region the bile-ducts, where not involved in the abscesses, were dilated, and some contained pus. The portal veins were never visible, being almost certainly the centres from which the abscesses had spread, i.e., the appearances suggest that the lesion was a pylephlebitis rather than a pure suppurative cholangitis (*see below*). The duodenum was opened *in situ*, and the mass which at the operation had appeared to be indenting the duodenum at the site of the head of the pancreas was found to be a firm papilliferous growth springing from the site of the biliary papilla (*Fig.* 267). It measured $2\frac{1}{4}$ in. in the line of the lumen of the gut, and 1 in. across, and projected $\frac{3}{4}$ in. into the lumen from a broad pedicle. The orifice of the ampulla of Vater was completely obliterated. Histologically the tumour proved to be a columnar-celled carcinoma with a papilliferous surface, arising from the intestinal mucosa lining the biliary papilla.

Fig. 267.—Photograph of the growth *in situ*. ($\times \frac{2}{5}$.)

Inflammation within the gall-bladder had subsided considerably following the cholecystostomy, and the whole operation area was free from gross infection. The common bile-duct was only moderately dilated, showed inflammatory congestion only, and did not contain pus; nor was there any obvious suppuration within the portal vein.

The kidneys showed a moderate degree of chronic fibrosis and of jaundice pigmentation. The lungs were affected by a patchy hypostatic pneumonia and marked œdema, the œdema fluid being bile-stained. The pancreas,

though firm and somewhat fibrotic, showed no malignant change or involvement; and the enlarged lymphatic glands found around its head showed acute inflammatory changes only.

COMMENT.

On the pathological side, the nature of the growth and the intrahepatic suppuration are of interest. The relatively large size of the lesion in this case, and the absence of involvement of the pancreas, rule out true Vaterian carcinoma, as also carcinoma of the duct of Wirsung and of the common bile-duct.

The appearance of the pylephlebitis within the liver without obvious suppuration in the extrahepatic portion of portal vein, though uncommon, is well recognized. In cases of this nature it is suggested that the primary lesion is an infective cholangitis and that abscesses form outside the ducts, possibly in the lymphatics. From these, suppuration spreads to the branches of the portal vein, whence a pylephlebitis follows with diffuse suppuration of the portal spaces in the liver.

Clinically the case presents several points of interest. The transient nature of the two earlier attacks of jaundice is contrary to much of the teaching in connection with malignant growths of or near the bile-passages. Rolleston,[1] however, in 1905 drew attention to this point, and stressed the fact that, while growths of the intestinal mucosa covering the biliary papilla were not common, they were particularly prone to produce an ascending infective cholangitis with intrahepatic suppuration. This resulted from, *inter alia*, the obstruction to the bile outflow, which in its turn was liable to intermissions following ulceration and necrosis of the growth. More recently Carnot (1928), quoted by Barron,[2] has similarly stressed the intermittent nature of the jaundice in tumours of the papilla of Vater. The importance of these considerations is obvious, as a recognition of this cause of intermittent jaundice is essential to the diagnostician who would assign a cause to a transient attack of jaundice occurring in elderly patients.

Other factors in this case which helped to cloud the diagnosis were the absence of any history suggestive of cholelithiasis, the failure to palpate the gall-bladder enlargement, and the absence of evidence of involvement of the pancreas. All these observations were in favour of a diagnosis of catarrhal jaundice; and probably the only factor against this diagnosis was the age of the patient.

The clinical course and operative and post-mortem findings in our case agree very closely with the observations of Cohen and Colp[3] (8 cases, 1927) and Wahl[4] (6 cases, 1924). The former of these authors, however, found that when infection of the tumour area occurred acute pancreatitis commonly ensued; and both authors emphasize the frequent occurrence of intestinal hæmorrhages. Neither of these conditions appeared in our case.

In conclusion we submit that a consideration of this case illustrates the following important points:—

1. It is wise to avoid the diagnosis of catarrhal jaundice in middle-aged or elderly patients.

2. Carcinoma of the duodenal mucosa covering the biliary papilla produces jaundice which is frequently characterized by its remissions.

3. While suppurative cholangitis is a frequent complication of these tumours, and cholæmic intestinal hæmorrhages are not uncommon, a rarer sequel is an intrahepatic suppurative pylephlebitis.

SUMMARY.

A case of carcinoma of the duodenal mucosa of the biliary papilla is reported.

The difficulties of the diagnosis of this condition are explained, and the importance of the feature of intermittent jaundice in elderly patients is stressed.

We are indebted to Dr. Bigland and to Mr. Hugh Reid for permission to publish this case.

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[2] BARRON, E. S. G., "Bilirubinæmia", *Medicine*, 1931, x, 1.
[3] COHEN, J., and COLP, R., *Surg. Gynecol. and Obst.*, 1927, xlv, 332.
[4] WAHL, H. R., *Med. Clin. N. Amer.*, 1923–4, 1348.

A FIBROMYOMA OF THE STOMACH WEIGHING OVER 2 LB.

BY A. J. BLAXLAND, NORWICH.

APART from its size, this tumour is of interest in that clinically it did not appear to be connected with the stomach, and it caused no obvious symptoms until necrosis developed in a portion of it.

HISTORY.—The patient, a man of 60, sent to me by Dr. Gaynor, of Wymondham, was known to have had a large swelling in the abdomen for at least two years. He had had some dyspepsia on and off for many years. On Dec. 10, 1930, he developed abdominal pain and pyrexia.

ON EXAMINATION.—Abdominal examination revealed a solid, semi-elastic, tender, rounded swelling, about the size of the head of a year-old child. Its centre was 2 in. to the right of the umbilicus and 1 in. below it. It was almost immobile.

OPERATION (Dec. 19).—Cœliotomy was performed. The tumour was found to lie in the lesser sac. The transverse mesocolon was adherent over an area on its lower aspect, where the wall of the tumour had become gangrenous (and a little stinking pus escaped on undoing these adhesions). Apart from this the tumour lay free in the lesser sac, except where it was attached over a width of 2 in. to the posterior wall of the stomach. An elliptical incision through the stomach wall around this attachment completed the removal of the tumour. Except for some suppuration in the lower end of the wound the patient made an uneventful recovery.

PATHOLOGY.—The tumour is now in the Museum of the Royal College of Surgeons. Sir Arthur Keith informs me that it is the largest specimen of its kind in the Museum. It weighs 2 lb. 6 oz., and is 7 in. across in its longest diameter.

Microscopic section confirms the naked-eye diagnosis of fibromyoma. The tumour was solid except for a small cavity in its centre, which communicated

FIG. 268.—Drawing of vertical section through the tumour, showing cavity in centre of growth. The arrow points to the attachment of the tumour to the posterior wall of the stomach, and shows the mucous membrane dipping down into the growth. The dark portion of the left-hand side of the growth is an area of necrosis. ($\times \frac{2}{3}$.)

with the lumen of the stomach by an orifice $\frac{1}{2}$ in. in diameter; and the mucous membrane of the stomach can be seen dipping down into this orifice (*Fig.* 268). In relation to the stomach wall the fibromyoma was entirely subperitoneal. The dipping in of the mucous membrane suggests that at an early stage of its growth the tumour was partly submucous and protruded into the lumen of the stomach.

REVIEWS AND NOTICES OF BOOKS.

Nasenplastik und sonstige Gesichtsplastik, nebst einem Anhang über Mammaplastik und einige weitere Operationen aus dem Gebiete der ausseren Körperplastik. By Prof. Dr. J. JOSEPH (Berlin). Imperial 8vo. Pp. 843 + xxxi, with 1718 illustrations, many in colour. 1931. Leipzig: Johann Barth and Curt Kabitzsch. RM. 242.

THIS monumental work is notable for its size, completeness, and the number and beauty of its illustrations. It begins with eighty photographic illustrations of the typical forms of defect in the nose, face, and breast, the treatment of which forms the bulk of the volume. A short chapter on the anatomy of the face is followed by a critical analysis of the face profile, giving angles and measurements which represent normal and abnormal variations. The profile of the nose is made up of three parts: the upper by the nasal bones, the middle by the septum and main nasal cartilages, and the lower by the nasal tip. Any one of these three parts may be altered by injury or disease in the direction of failure or excess, and forty-one outline drawings are given of the possible variations in the profile of the nose. A short section on biological principles of the survival and growth of transplants, both skin and bone, is followed by the most important part of the book dealing with the fundamental principles of plastic surgery.

In the majority of the operations anæsthesia is obtained by the use of local infiltration by a 1 to 2 per cent solution of novocain combined with adrenalin, but general inhalation anæsthesia is used for children and nervous adults. As regards apparatus and instruments, the technique is remarkably simple and unencumbered with special tools. There are, of course, specially shaped saws and raspatories for intranasal use, but for the taking of bone-grafts for the face a simple bow saw or a Gigli saw is used.

One of the most interesting chapters is that which describes the re-shaping of large or ugly noses, and this part lends itself especially well to the most intriguing illustrations of how ugly people are made beautiful. The large humped nose is reduced by subcutaneous and submucous resection of either the bridge or the nasal walls. Deformities of the alæ and the tip of the nose are corrected by excision of or addition to the cartilage of these structures. Loss of the whole or part of the nose is by far the most important problem of nasal plastic surgery. A full historical account is given of this subject with a short review of the various methods which have been used up to the present day. We think that in this and in subsequent sections the methods of tube-flap which the work of Gillies has made so familiar to us are not recognized as fully as they deserve. For the most part the methods advocated are those of the pedicle flap from the arm, which is recommended chiefly for women and in cases in civil practice; and the pedicle flap from the forehead, which is more suitable for men and for war surgery.

It is quite impossible to do justice to a work of this size in a short review, and one can therefore only touch upon one or two outstanding points. In the reconstruction of total loss of the nose, there are three main structures to be provided: the septum is provided by a free graft from the tibial crest, which is first implanted into the lip and then raised into position; the lining of the nose is provided by cheek-flaps; and the outer skin by the classical flap from the forehead. In cutting the tibial graft a bow saw is used, and it is remarkable how very little in the way of special instruments is recommended.

The remainder of the work deals with the plastic operations for damaged eyelids, lips, and cheeks, the operation for facial paralysis, the reconstruction of the jaws, the external ears, and the raising and reducing of hypertrophied pendulous

breasts. In facial paralysis, the usual nerve anastomosis operations are described, but also some ingenious plastic devices for supplementing the facial muscles by slips taken from the temporal and masseter muscles. In the reconstruction of the proximal part of the lower jaw, one of the metatarsal bones is used, making use of the head of the latter as the condyle of the jaw. To make good the loss of the external ear, a model is made of thin ivory, perforated with many holes. This is implanted in suitably placed skin-flaps which are finally swung into position.

The completeness of this work on plastic surgery, and the great wealth of illustrations make it an invaluable book of reference, and afford a wonderful testimony to the industry of its author and the high standard of its publisher.

Collected Papers 1904–1929. By EDWIN BEER, M.D. (New York). Large 8vo. Pp. 827 + xii, with 252 illustrations. 1931. New York: Paul B. Hoeber Inc. $7.50.

PERHAPS the most remarkable feature of this book is the diversity of subjects which the author has studied during the period under review, such as the causes of gall-stones, the pegging of fractures, the removal of a foreign body from the bronchus, and a long study of urinary diseases. The majority of the subjects are treated in a masterly manner. It is notable that there is perhaps an element of closer personal contact with the literature in the earlier papers than in some of the later ones. In general it may be said that there is evidence of a greater expenditure of time on the part of the author in the earlier papers than he has found possible to give to the later ones. For instance, the chapter on diverticula of the intestine (1904) is informative, well constructed, and deals with all aspects of the subject. Many of the author's own experiments are recounted. By comparison the paper on chronic tubercular kidney (1921) is rather more in the nature of an article in a text-book. One advantage of the book is that the bibliography fills the gap so often missing in more recent articles on surgical subjects. The chapter on the significance of diarrhœa following abdominal operations (1923) calls attention to a subject of clinical interest and value. Although well known and taught to students many years before the author's first observations of it, it is none the less profitable to read. The consideration of intrahepatic cholelithiasis in another chapter is well conceived.

One great value in any collection of papers is that the progress of any particular subject in the author's mind will frequently reveal its position in the profession as a whole, especially when the papers have been read in the opening of discussions at societies. Such papers as those on cryoscopy and on renal tests in general should perhaps have been referred to and correlated with the author's more mature experience in the 1928 paper. Had he given us from the many thousands of tests which he has performed his definite conclusions as to whether the nitrogenous excretion goes hand in hand with the excretion of dyes he would have greatly added to our knowledge and enabled us to retain the essential tests and discard the others. He writes, "The student of functional tests, however, appreciates the dangers which he is facing, whereas prior to these tests there was failure to realize how thin the ice was." The animal experiments on renal function (1912) are particularly interesting, and technically the author's method of catheterizing both ureters in a child at the same time by employing a single catheterizing cystoscope and two whalebone guides is ingenious. One would like to have his experience of the method since the date of publication (1911), for, as so often happens, it may be impossible to pass even a small cystoscope when there is a catheter already present in the urethra.

There is, as may often happen in a collection of papers, a large amount of repetition—for instance, 167 pages are devoted to tumours of the urinary bladder. In these an illustration of the use of a rubber hot-water bottle as part of the drainage system is repeated on pages 364, 382, and 462, and diagrams of currents used for coagulation and illustrations of the technique of removing growths of the bladder are often repeated. Were it possible, in a future edition, to replace these chapters by one arranged in chronological order quoting the articles and setting forth the author's views at different periods of his experience, repetition would be replaced

by brevity and erudition. The author's enthusiasm for surgery is evidently not waning, judging from the manner in which in 1926–8 he sets forth the development and progress of the surgery of the spleen and associated blood diseases.

Throughout the work the illustrations are clear and well reproduced. The patient applying a hot-air douche for sciatica appears to be turning it away—perhaps because it was too hot! The typography is clear, the style often forcible and always lucid, misprints are few, but the index is insufficient. There is a whole chapter dealing with lime deposits in the kidneys, yet the words 'lime', 'chalk', or 'stone' are not mentioned in the index. This collection of papers as a whole is excellent and well repays perusal.

Minor Surgery and Bandaging for the Use of House Surgeons, Dressers and Junior Practitioners. By GWYNNE WILLIAMS, M.S., F.R.C.S., Surgeon, University College Hospital. Twentieth edition. Crown edition. Pp. 445 + viii, with 262 illustrations. 1930. London: J. & A. Churchill. 10s. 6d. net.

WHEN a book has reached a twentieth edition it is quite superfluous to extol its merits, which in this case have been appreciated more and more since its first appearance in 1861. On the other hand, one feels more justified in making criticisms with the hope that the character and usefulness of the work may be still further improved. Our first criticism is to express surprise at the original authority of the book having been suppressed. Surely a book which was planned and written by Christopher Heath should still show his name somewhere on the title-page?

The present edition has been revised throughout, particularly in the chapters about the treatment of fractures and the administration of anæsthetics. The descriptive matter on the treatment of fractures is clear and sound, but for an up-to-date book we think more care should have been taken with illustrations. For example, *Fig.* 181 is not Hey Groves's, but Borchgrevink's, humerus splint, and is probably quite obsolete. *Fig.* 209, showing the suspension treatment of fractured femur in a child, depicts each leg fixed to a back splint and the two back splints fixed to each other. Surely the effect of suspension will be much more efficient if no splints are used? Skeletal traction can be applied by many methods, but why choose the least simple and efficient of these (*Figs.* 215 and 216) in depicting long screws driven into the bones, rather than the transfixion pin or the taut wire? Of all the Thomas splints, those for the hip and the knee figured in *Figs.* 237 and 241 are almost obsolete, but the walking caliper splint is not mentioned. In the section on anæsthetics, we think that undue space is given to chloroform and to the Vernon Harcourt apparatus. All these points are, however, only minor matters, and we have no doubt that the book will continue to be the *vade mecum* of the present and future generations of dressers and house surgeons.

Surgery: its Principles and Practice. For Students and Practitioners. By ASTLEY P. C. ASHHURST, A.B., M.D., F.A.C.S., Professor of Clinical Surgery in the University of Pennsylvania. Fourth edition, thoroughly revised. Large 8vo. Pp. 1189 + xii, with 1063 illustrations and 15 coloured plates. 1931. London: Henry Kimpton. 45s. net.

THIS new edition of the well-known American text-book follows closely on the third edition which was reviewed scarcely three years ago in these pages. It may be compared with the new *Rose and Carless*, which it resembles closely except that it is somewhat less bulky—1100 pages as against 1500. The text is clear, concise, and dogmatic. The illustrations are photographic and for the most part original. Among re-written matter there are interesting sections on myelomata, injection of varicose veins, thrombo-angiitis obliterans, spinal anæsthesia, diathermy, hyperthyroidism, etc. The information is therefore quite recent and sound. The chapters on orthopædic surgery are especially full. It is deservedly one of the most popular text-books for American students.

Thomson and Miles' Manual of Surgery. By ALEXANDER MILES, M.D., LL.D., F.R.C.S. (Ed.), Consulting Surgeon, Royal Infirmary, Edinburgh; and D. P. D. WILKIE, M.D., F.R.C.S. (Ed. and Eng.), Professor of Surgery, University of Edinburgh. Vol. I. General Surgery. Eighth edition. Crown 8vo. Pp. 574 + xvi, with 176 illustrations. 1931. London: Oxford University Press. 12s. 6d. net.

IN welcoming the eighth edition of this well-known text-book of surgery, the most important change to be noted is that Professor Miles has Professor Wilkie associated with him as joint editor of the work. The task of editing such a text-book and seeing that its various sections are kept up to date can be no light one, especially when the book has for many years been associated with the Edinburgh School and its traditions, and the sacrifice of a section of doubtful value might be considered sacrilegious disregard for hallowed memories. It is stated in the preface that the editors have endeavoured to avoid adding to the size of the work, and doubtless were it not for that endeavour the book would be very much larger even than it is.

Yet it would appear that if it were possible to remodel the whole work it could be contained in a smaller compass. A great many chapters at present contain material that has been dealt with in other sections, and this applies especially to pathology. Every contributor in dealing with his own subject must give an account of the pathology of the conditions the clinical course of which he is about to describe. This being so, the introductory chapters need to contain only the fundamental outlines of pathology, and no therapeutics, leaving the details of pathological processes occurring in the special tissues and their treatment to the sections dealing with the particular organs themselves. This would prevent overlapping and avoid confusion, and there would be no fear that the student would grow up ignorant of pathology, for he has now become accustomed to seek for special information in this vast field in text-books devoted to the subject.

This criticism may be more readily understood if examples of such redundancies are mentioned. In the introductory chapters dealing with acute inflammation, acute infections of the skin and their treatment are described in detail, and they are again set forth in the chapter on diseases of the skin. Incidentally the processes of the formation of a boil and the formation of a carbuncle are not distinguished, a carbuncle being described as a collection of boils. In the chapter on tumours, the tumours of bone are described, and the descriptions are repeated under diseases of bone, even the atypical skiagram corresponding to the atypical pathological specimen being used to illustrate the account of benign giant-cell tumour!

To show how a student may be confused by two accounts of the same thing, we may quote from the chapter on gangrene: "The occlusion of the vein as well as the artery (by ligature) is not found to increase the risk of gangrene"; and from the chapter on injuries of blood-vessels, "When ligation of the artery is necessary, the risks of gangrene are diminished by ligation of the corresponding vein". Repetition is unavoidable in a work composed of the writings of several contributors, and we sympathize with the editors in their thankless task of choosing that which is more excellent.

The standard of the work as a whole is as high as ever, the descriptions of tuberculous disease and of burns, and the general account of the inflammatory diseases of bone, being perhaps especially noteworthy. The book retains its well-known form, and will easily retain also the affection of those who have grown up and are growing up with it.

Crippled Children: their Treatment and Orthopedic Nursing. By EARL D. MCBRIDE, B.S., M.D., F.A.C.S., Instructor in Orthopedic Surgery, University of Oklahoma Medical School. Large 8vo. Pp. 280, with 159 illustrations. 1931. London: Henry Kimpton. 15s. net.

THE care of crippled children requires the services of a composite team including surgeons, nurses, physiotherapeutists, and social workers. Dr. McBride has written a simple, non-technical manual designed primarily for nurses and other lay assistants. It should be a very useful book, for it keeps to simple and sound principles, avoiding details of particular methods in which the work of one surgeon may well

differ from that of others. English surgeons need feel no hesitation in recommending this book to their nursing staffs and other lay assistants; for, although it is written by an American, the methods of treatment considered differ little from those in common use in English orthopædic hospitals and clinics. The illustrations give examples of most of the common crippling conditions of childhood. They are good in themselves and well reproduced—in fact, the book is open to practically no criticism and serves the purpose for which it is designed in an admirable manner.

Die Chirurgie. A System of Surgery. Edited by Profs. M. KIRSCHNER (Tübingen) and O. NORDMANN (Berlin). Fasc. 30 (Index). Royal 8vo. Pp. 219 + vii. 1930. Berlin and Vienna: Urban & Schwarzenberg. Paper covers, RM. 12; bound, RM. 14.

THIS is the last section of a great work and is entirely a series of indexes. The first is a list of the sixty-six contributors to the work. The next is a register of the contents of the six volumes. This register occupies 58 pages and deals with the contents of nearly 9000 pages. Lastly there follows an alphabetical index of subjects and authors, occupying 149 pages.

Each section of this work has been reviewed in these columns, and it only remains here to offer our warm congratulations to the editors, contributors, and publishers for the production of what is probably the largest and most authoritative work on surgery ever produced. It is, of course, a German work, and for that reason it has merits and drawbacks of its own. It forms a most valuable reference work, representing German practice and teaching, but we think that it does not give an equally authoritative exposition of French, American, and British surgery. But to put against this limitation, there is the fact of the very extensive bibliography which accompanies every chapter. The exposition of the theory of surgery and its pathological basis is perhaps the outstanding feature of the book, rather than the practical discussions on treatment. Our greatest admiration is for the team spirit, which has enabled so many to collaborate in producing such a monument of industry and research.

Operative Chirurgie der Knochenbrüche. By Professor FRITZ KÖNIG (Würzburg). Vol. I. Operationen am frischen und verschleppten Knochenbruche. Royal 8vo. Pp. 194 + vi. Illustrated. 1931. Berlin: Julius Springer. Paper covers, RM. 27; bound, RM. 29.80.

THIS is a short and concise work, well illustrated, and written by a master hand of great experience. In regard to the vexed question of the indications for open operation, the author protests against the commonly accepted teaching that the procedure should be reserved for cases in which more conservative methods have failed. But he refers in his argument to those cases of mal-union in which inefficient methods have been persisted in far too long. Well-applied skeletal traction ought to give full length, good alinement, and sufficient apposition within ten days of its initiation, and then if it has failed there is no hindrance to open operation, but rather a great help. We feel sure that this is the solution of this difficult problem. For anæsthesia, local infiltration with ½ per cent novocain solution is recommended for the majority of recent fractures, but general anæsthesia is used for the fractures of the femur.

The bulk of the book is occupied by detailed descriptions of operations upon special fractures, and follows very closely the methods of plating with which Lane's work has made us familiar. The author discusses on very sound lines the question of the influence of foreign bodies buried in the tissues. It is not so much the danger of sepsis that is to be feared as the interference with the circulation in the bone and periosteum. Nevertheless the great bulk of the work is occupied with a description of plating operations, whereas removable agents—e.g., transfixion pins—or absorbable agents—e.g., bone-pegs—are hardly mentioned. We shall await with much interest the further volume dealing with old mal-united or ununited fractures.

Verlauf der wichtigsten Knochen- und Gelenkerkrankungen im Röntgenbilde. Eine anschauliche Prognostik. By Privatdozent Dr. med. VICTOR HOFFMANN, Oberarzt der chirurgischen Universitätsklinik im Augusta-Hospital zu Köln. English and German text. Imperial 8vo. Pp. 264 + x, with 584 illustrations. 1931. Berlin: Julius Springer. Paper covers, RM. 66; bound, RM. 69.80.

THIS work is one of outstanding merit, and the fact of its presentation in English as well as German makes it of great value to us for purposes of reference. A series of 156 severe cases of bone and joint disease is presented, and of each case three to five X-ray pictures are given at different stages showing the progress of the disease. The subjects dealt with are: acute and chronic osteomyelitis, both hæmatogenous and traumatic, new growths, nutritional and metabolic diseases, rheumatism and osteo-arthritis, fractures and their complications, bone-grafting, and arthroplasty.

We have nothing but praise for the book, which in a small compass puts together in a graphic form the whole story of bone and joint disease. We hope that in further editions a greater space will be devoted to the subjects of tuberculous disease of the spine and larger joints, which present themselves in such great variety as to require more examples.

It would perhaps seem ungracious to criticize the English text, which is perfectly clear and intelligible, but it would be worth while to have this revised by an English surgeon so as to make it conform with English phrasing and wording. For example, we speak of the 'involucrum' and not of the 'coffin', of 'arthroplasty' and not 'joint plasty', and so on. We think the book is one which every surgeon should have for reference.

Injuries to Joints. By Sir ROBERT JONES, Bart., K.B.E., C.B., Ch.M. (L'pool), F.R.C.S. (Eng., Irel., and Edin.), F.A.C.S., Emeritus President, British Orthopædic Association, etc. Third edition. Pott 8vo. Pp. 195. Illustrated. 1930. London: Humphrey Milford. 6s. net.

WE are glad that this small book of wisdom remains with us and is brought up to date. It was born in the war (1915), and the first two editions have had to be reprinted ten times. The value of the book consists in the two facts of the experience of its author and the essential simplicity of its teaching. The present edition has been revised and brought up to date; the section on ischæmic paralysis has been rewritten. In this revision the author acknowledges the help of Mr. Harry Platt.

Chirurgia del Dolore. La Chirurgia della Innervazione periferica del Simpatico. By Prof. IGNAZIO SCALONE. Medium 8vo. Pp. 254 + xvi, with 99 illustrations. 1931. Milan: Ulrico Hoepli. L. 30.

THE surgery of pain is a difficult subject upon which to write a good book. There is wheat in Professor Ignazio Scalone's pages, but it is difficult to sift it from the chaff. The main thesis seems to be that peri-arterial sympathectomy has failed of its promise because perineural sympathectomy, its true counterpart, has been neglected. The author advocates treatment of nerve-trunks just as Leriche treats arteries. He admits that the anatomical, histological, and physiological bases of his technique are still rather nebulous. A very considerable part of the work recapitulates the research and practice of other surgeons, and records experiences differing but little from the generality.

With Raynaud's disease, and the various forms of arteriosclerosis and end-arteritis, Professor Scalone has had a certain success, some equivocal amelioration, and some failure, very much where others have found them. He has an interesting chapter devoted to causalgia and like states; his descriptions are reminiscent of the pages of Madame Athanassio-Benisty (some of whose figures he reproduces with acknowledgement, though her name does not appear in the bibliography) written during the prevalence of war injuries of nerves.

In his eighth chapter the author deals with various forms of pelvic neuralgia of uncertain type; his anatomical elucidations seem rather fanciful, and his case

records carry little conviction. The section is open to the criticism, equally applicable to the subject of the next chapter, renal neuralgia, that the 'neuralgic' element is inseparable in most instances from organic disease of the parts, which calls for and receives treatment at the same time ; whilst diagnosis, at the early stage he considers desirable for cure to be likely, must be very difficult and uncertain. In some sections—for example, that on aclasia—the description of the sympathetic innervation concerned is followed by nothlng specifically related thereto in the operations described—nothing more, that is, than the interference incidental to the operations ordinarily performed. A chapter is devoted to speculations on the part played by inflammation of the sympathetic system in obscure painful abdominal states. To technique is devoted half a dozen pages. Forty-four cases are described at length, but some of them have no very close relation to the subject-matter.

The sub-title of the book is " The Surgery of Peripheral Sympathetic Innervation". Afferent sympathetic fibres are traced from the periphery to blood-vessels and thence to the trunk of mixed nerves ; the efferent nerve paths are figured as, in the main, avoiding these trunks. It is understandable, therefore, that the author should emphasize the importance of dealing with such efferent fibres in the adventitia of the main nerve-trunks, and have less to say about attack on the ganglia rather than the vascular adventitia, which has been the recent tendency of many surgeons.

Considering the difficulty any one surgeon has in getting enough of these rare cases of his own to form an adequate body of personal documents, it would be unfair to close without praise for the patience and enthusiasm that have gone to the production of this book, or to leave the impression that it will not be of considerable value to those with enough clinical experience to discern the sound work from the padding.

Practical Methods in the Diagnosis and Treatment of Venereal Diseases for Medical Practitioners and Students. By DAVID LEES, D.S.O., M.A., M.B., D.P.H., F.R.C.S., M.R.C.P. (E.), Surgeon in Charge of Venereal Diseases, Royal Infirmary, Edinburgh, etc. With an Introduction by WM. ROBERTSON, M.D., F.R.C.P., D.P.H., Late Medical Officer of Health, Edinburgh. Second edition. Crown 8vo. Pp. 634 + xx, with 87 illustrations. 1931. Edinburgh : E. & S. Livingstone. 15s. net.

THE fact that a second edition of this work has been called for so speedily indicates that it appeals to a definite and appreciative class of reader—the class that requires a full and accurate account of these diseases, clear indications as to treatment, and, above all, reasoned grounds on how one may arrive at a reliable prognosis. Dr. Lees's book supplies all these desiderata. It is a typical example of what one would expect from the Edinburgh School of Medicine.

The author does not think he can cure primary Wassermann-negative syphilis in six months. He insists on the traditional two years of the combined arsenic-bismuth (or mercury)-iodide treatment. Nor does he utterly contemn mercury as useless, like many of those trained in the Continental school of thought. This is typical of his cautious attitude towards recent and untried opinion.

Naturally no two persons' experience or opinions ever quite coincide. When speaking of expectant mothers, we find him writing : " It is advisable to give such infected mothers the benefit of the treatment in every subsequent pregnancy." We would like to substitute for 'advisable', '*imperative*'. We note with approval his remark that it is the cases of neurosyphilis which practically never have any discomfort after lumbar puncture ; but we are somewhat surprised at the warm manner in which he advocates tryparsamide in this condition, as our experience has not been so happy. We are also surprised to find that in malariotherapy, he allows only ten to twelve rigors to occur before checking with plasmoquin. Few alienists are now satisfied with less than three or four courses of rigors, checked by intervals produced by quinine.

Turning to the treatment of gonorrhœa, we note with pleasure that the author advocates perineal incision in prostatic abscess, instead of the old barbarous practice of rupturing it into the prostatic urethra with a sound (a line of treatment which can be guaranteed to keep up the discharge for many months) ; but we regret to find

that he thinks a peri-urethral abscess should be opened into the urethra, and not by incision through the skin. On page 540 the text suggests, probably inadvertently, that stricture of the membranous urethra is common as a complication of gonorrhœa, whereas it is practically non-existent except as the result of trauma. The remarks on the fetish of douching in gonorrhœa in women, and on the over-emphasis of diathermy as a curative agent, are very salutary.

In a work in which so many figures occur there are bound to be errors, even with the most careful proof-reading. Most of these will be obvious to the reader, but the statistics on page 271 seem quite incomprehensible.

Finally, a word about the illustrations. These are frankly disappointing. The essential parts shown are too small or too blurred to be of much use. Instead of 'close-ups' of the lesions, we have half the bodies of the patients. Here we touch on what appears to be an essential difference between the British and the American publisher. The American publisher sees that he gets good scale illustrations, either from a skilled professional artist or photographer. He produces the work superbly; and after one has bought it, tempted by the illustrations, one often finds the text quite unworthy of its setting. We appear to err in exactly the opposite way. The text is generally beyond reproach in English medical works, the illustrations are often quite inadequate.

Dr. Lees has produced a work which is accurate, balanced, and well written. It is a mine of up-to-date information on all things venereal. We regret that he has not been better served by his illustrators, and hope that when the next inevitable edition comes along, he will see that more justice is done to his admirable letterpress.

Die Avertinnarkose in der Chirurgie. By Professor D. W. Anschütz, Direktor der Chirurg. Klinik, Kiel; Dr. K. Specht, Assistent der Chirurg. Klinik, Kiel; and Priv.-Doz. Dr. Fr. Tiemann, Assistent der Mediz. Klinik, Kiel. Royal 8vo. Pp. 200, with 9 illustrations. 1930. Berlin and Vienna: Julius Springer. RM. 16.50.

This book is written by two surgeons and a physician. It is the first attempt to crystallize the experience of surgeons in Germany in book form, and is written with characteristic national thoroughness. The earlier chapters deal with the history and development of avertin narcosis, and with the chemistry and pharmacology of the drug, the latter section being exhaustive. In discussing dosage, the authors are careful to point out that there is no invariable rule-of-thumb method for calculating the correct dose from the body weight. They consider the real criterion to be the metabolic rate of the patient, taking into consideration such factors as age, amount of fat present, nervous state, and so on. The intravenous method of administration is discussed, but is not recommended, the method for most cases being the giving of a single dose per rectum.

A chapter is devoted to the discussion of the degree of narcosis to be aimed at, and the conclusion of the authors is that in 50 to 60 per cent of cases at the present time full anæsthesia can be obtained. The ultimate aim is to produce this in all cases, and the authors express the hope that with refinements of technique this will be possible before long. This is a conclusion with which most anæsthetists in this country will not agree, holding that basal narcosis is the only result which is desirable and safe. It must be remembered that in most German centres anæsthetics as a speciality does not exist, and that these are therefore the ideas of surgeons who are either responsible for their own anæsthetics, or who are deputing the task to more or less unskilled assistants. In those cases in which supplementary anæsthesia is required, the authors regard ether as the anæsthetic of choice, and have no personal experience to give of gas and oxygen.

Finally, 103 cases are analysed in which death followed the giving of avertin. In 74 of these cases avertin is entirely cleared of blame for the fatal result, while of the remaining 29, 17 are described as very doubtful and 12 as possible. The authors profess themselves unable to draw any conclusions from these figures, but assess the mortality-rate at 1 in 10,000 cases. In all these cases the dosage used was considerably in excess of that generally employed in this country. A short section is

devoted to the use of avertin in tetanus, with apparently encouraging results. There is no mention of the use of avertin in obstetrics, a subject on which several papers have appeared in Germany.

Le Traitement médico-chirurgical de l'Occlusion intestinale aigue et subaiguë. By PIERRE MOIROUD (Marseilles). Crown 8vo. Pp. 122. 1931. Paris: Masson et Cie. Fr. 18.

THIS small brochure of 120 pages is one in a series "Médecine et Chirurgie Pratiques", published by Masson et Cie. It is in the form of a rather expanded paper without illustrations, and it reviews the more recent work on the indications, technique, and results of acute intestinal obstruction; hernia and cancer of the bowel are excluded. A very complete account is given of obstruction by bands, intussusception, gall-stone, volvulus, Meckel's diverticulum, etc., but the main interest of the book lies in the discussion on paralytic ileus. This most distressing sequel to an abdominal operation is fully considered by the author in the light of modern research. He has arrived at definite conclusions which should be borne in mind by all surgeons. These conclusions are as follows: (1) The value of an abdominal X-ray without barium; (2) The importance of re-hydration of the patient; (3) The re-chlorination of the blood by intravenous hypertonic saline (20 c.c. of a 10 per cent saline every four hours); (4) Lavage of the stomach; (5) Serotherapy by anti-Welchii serum; (6) The mechanical emptying of the greatly distended small bowel by aspiration; (7) The great importance of spinal anæsthesia. The book is most clearly written, and is well worth perusal by all abdominal surgeons.

Der appendicitische Anfall: seine Ätiologie und Pathogenese. By LUDWIG ASCHOFF (Freiburg-i.-Br.); mit einem kurzen Beitrag über die Lymphgefässverhältnisse am menschlichen Wurmfortsatz, by Dr. H. SENG. Medium 8vo. Pp. 125. with 36 illustrations. 1930. Berlin and Vienna: Julius Springer. Paper covers, RM. 12.40; bound, RM. 14.

THIS short discussion on the etiology and pathology of appendicitis by the distinguished German pathologist is perhaps disappointing because of its limitations. We had hoped to find some new suggestion concerning the still unexplained incidence of the disease. The monograph, however, is full of valuable information and very good illustrations. Dr. Seng gives some new and remarkable pictures of the lymph-vessels of the appendix.

A large proportion of the book is occupied in a discussion of the bacteriology of appendicitis which does not seem to have any very practical bearing. An interesting estimate is given of the time periods occupied by the different phases in appendicitis. The primary infection takes twelve hours, ulceration occurs in twelve to twenty-four hours, phlegmonous inflammation following ulceration matures in twenty-four to forty-eight hours, and perforation or gangrene are events which occur after the forty-eight-hour period. Great stress is laid on the frequency of latent infection of the appendix, and for this reason it is advised that this structure should always be removed if possible when the abdomen is opened for any other purpose.

BOOK NOTICES.

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest for our readers.]

Schmerzverhütung: Zwölf Vorlesungen. By Dr. FRITZ STARLINGER (Vienna). Medium 8vo. Pp. 106 + vi. 1931. Vienna: Julius Springer. RM. 6.60.

Die Indikationen zum abdominellen Kaiserschnitt für alle Kaiserschnittoperateure. By Prof. Dr. GEORG WINTER (Königsberg). Royal 8vo. Pp. 124 + viii. 1931. Stuttgart: Ferdinand Enke. Paper covers, RM. 8; bound, RM. 9.60.

The Rational Treatment of Varicose Veins and Varicocele. By W. TURNER-WARWICK, M.A., M.B. (Cantab.), F.R.C.S., Surgeon to Outpatients and Surgeon in charge of the Rectal Department, the Middlesex Hospital, London. Crown 8vo. Pp. 188, with 12 illustrations. 1931. London: Faber & Faber. 5s. net.

The Ætiology of Irregularity and Malocclusion of the Teeth. Four lectures by Prof. J. C. BRASH, M.C., M.A., M.D. (University of Birmingham). With an Appendix "Concerning Orthodontic Problems and their Solution," by Miss M. L. TILDESLEY. Royal 8vo. Pp. 274 + xii, with 195 illustrations. 1931. London: Dental Board of the United Kingdom. 5s. net.

Chirurgie de l'Ulcère gastrique et duodénal (Indications. Résultats). By N. HORTOLMEI, Professeur de Clinique chirurgicale; and VL. BUTUREANU, Maître de Conférences, Faculté de Médecine de Jassy. Medium 8vo. Pp. 408, with 75 illustrations. 1931. Paris: Masson et Cie. Fr. 45.

A Short History of Anatomy. By RICHARD H. HUNTER, Ph.D., M.D., M.Ch., Lecturer in Anatomy, Queen's University, Belfast. Second edition. 1931. Crown 8vo. Pp. 88. 1931. London: John Bale, Sons & Danielsson Ltd. 3s. 6d. net.

Surgical Pathology of the Diseases of Bones. By ARTHUR E. HERTZLER, M.D., Professor of Surgery, University of Kansas. Hertzler's Monographs on Surgical Pathology. Royal 8vo. Pp. 272 + xiv, with 211 illustrations. 1930. London: J. B. Lippincott Co. 21s. net.

Chirurgie du Rectum. By HENRI HARTMANN, Professeur de Clinique chirurgicale, Chirurgien de l'Hôtel-Dieu. Imperial 8vo. Pp. 398, with 161 illustrations. 1931. Paris: Masson et Cie. Fr. 75.

Annals of Roentgenology: a Series of Monographic Atlases. Edited by JAMES T. CASE, M.D., Professor of Roentgenology, North-western University Medical College, Chicago. Volume VII, Urological Roentgenology. By HUGH H. YOUNG, M.D., Clinical Professor of Urology, Johns Hopkins University; and CHARLES A. WATERS, M.D., Associate in Clinical Roentgenology, Johns Hopkins University. Second edition revised. Large 4to. Pp. 564 + xlix, with 592 illustrations. 1931. New York: Paul B. Hoeber Inc. $20.00.

Congresos Argentinos de Cirurgia. Second congress, Buenos Aires, 1930. President: Dr. Eduardo Belaustegui. Super royal 8vo. Pp. 1140 + lxvii, with 249 illustrations. 1930. Buenos Aires: A. Guidi Buffarini. No price given.

Die Elektrochirurgie. By Prof. Dr. FRANZ KEYSSER (Berlin). Royal 4to. Pp. 238 + x, with 232 illustrations. 1931. Leipzig: Fischers Medizinische Buchhandlung. Paper covers, M. 52; bound, M. 56.

Operative Surgery: General and Special Considerations. By Dr. MARTIN KIRSCHNER (Tübingen), authorized translation by I. S. RAVDIN, B.S., M.D. (Philadelphia). Super royal 8vo. Pp. 666 + xii, with 746 illustrations, mostly coloured. 1931. London: J. B. Lippincott Co. 50s. net.

Physical Signs in Clinical Surgery. By HAMILTON BAILEY, F.R.C.S., Surgeon, Royal Northern Hospital, London. Third edition, revised and enlarged. Medium 8vo. Pp. 277 + xx, with 318 illustrations, some of which are in colour. 1931. Bristol: John Wright & Sons Ltd. 21s. net.

Die spezielle Chirurgie der Gehirnkrankheiten. Edited by Prof. FEDOR KRAUSE. Vol. II, Part 1—Die epileptischen Erkrankungen, by Prof. FEDOR KRAUSE and Dr. HEINRICH SCHUM (Berlin). Royal 8vo. Pp. 520 + xx, with 112 illustrations. 1931. Stuttgart: Ferdinand Enke. Paper covers, RM. 78; bound, RM. 81.

Maligne Pharynx- und Larynxtumoren. By A. ZUPPINGER, with a Foreword by H. R. SCHINZ. Large 4to. Pp. 188, with 33 illustrations and 9 plates. 1931. Leipzig: George Thieme. Paper covers, M. 28; bound, M. 30.

Proctoscopic Examination and the Treatment of Hemorrhoids and Anal Pruritus. By LOUIS A. BUIE, B.A., M.D., F.A.C.S., Associate Professor of Surgery, the Mayo Foundation, University of Minnesota. Mayo Clinic Monographs. Medium 8vo. Pp. 178, with 72 illustrations. 1931. Philadelphia and London: W. B. Saunders Co. 16s. net.

Collected Papers of the Mayo Clinic and the Mayo Foundation. Edited by Mrs. MAUD H. MELLISH-WILSON, RICHARD M. HEWITT, M.A., M.D., and MILDRED A. FELKER, B.S. Vol. XXII, 1930. Medium 8vo. Pp. 1125, with 234 illustrations. 1931. Philadelphia and London: W. B. Saunders Co. 60s. net.